THE

REPORT

OF THE

DEPARTMENT OF PATHOLOGY

OF

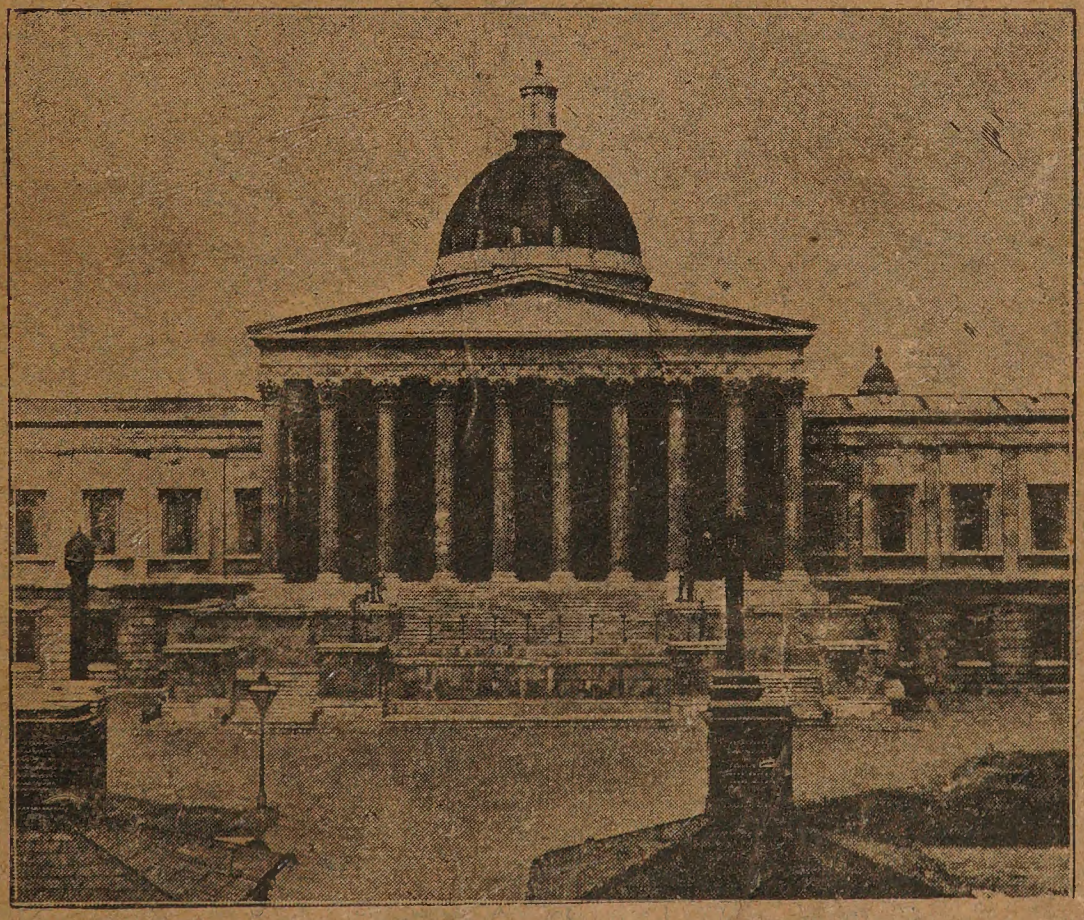
UNIVERSITY COLLEGE, LONDON.

June, 1895.

TOGETHER WITH A

COLLECTION OF PAPERS AND ABSTRACTS PUBLISHED FROM THE LABORATORY

VOL. V.



(UNIVERSITY COLLEGE, LONDON).

EDITED BY

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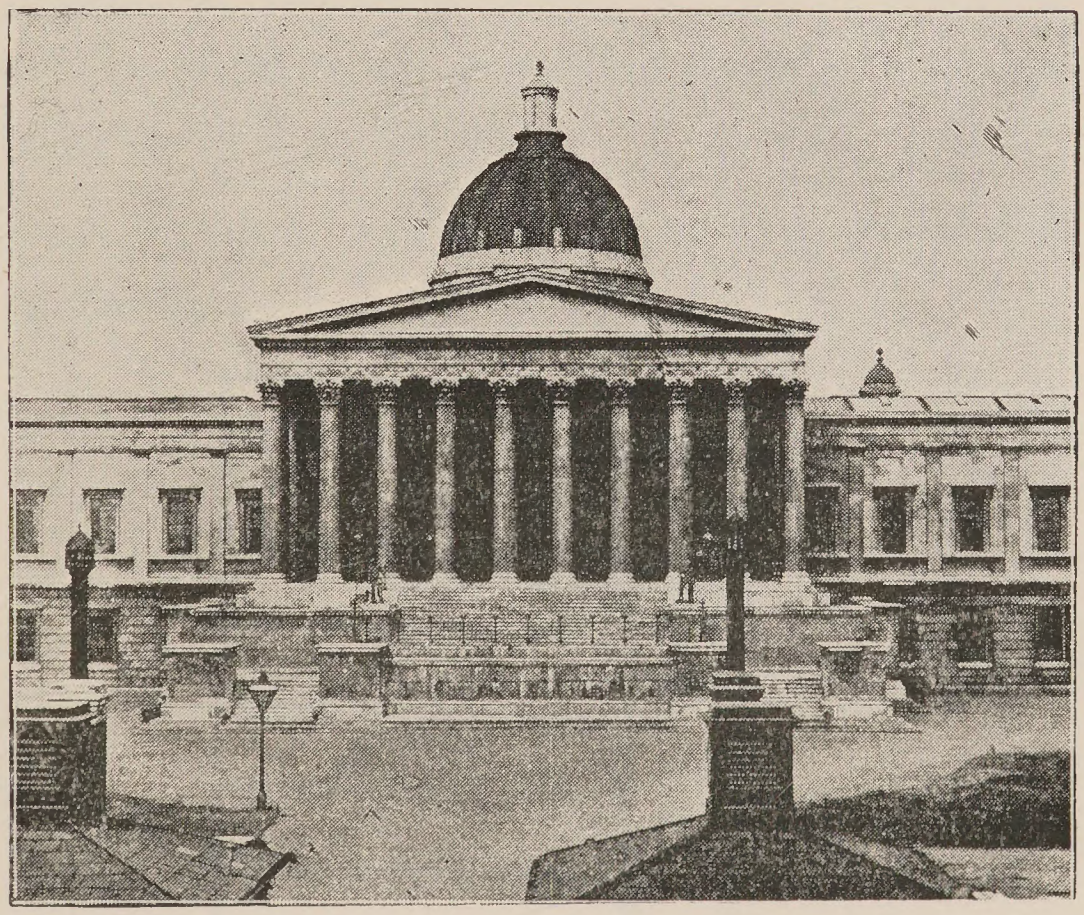

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INTRODUCTION.

The present volume forms the fifth of the series of collected papers which has appeared from the Laboratory, and is the fourth in the series of collected small papers and abstracts. The volume published in December, 1894, and consisting wholly of papers published in the Philosophical Transactions, was prepared separately on account of the size of the page of the Transactions.

It is intended to issue a similar volume as soon as sufficient papers shall have accumulated.

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J. S. RISIEN RUSSELL, M.D., M.R.C.P. — "On the Value of Experimental Evidence in the Diagnosis of Diseases of the Cerebellum." Brit. Med. Journal, May 18th, 1895.

J. S. RISIEN RUSSELL, M.D., M.R.C.P.—"Defective development of the Central Nervous System in a Cat." Brain, Part 1, 1895.

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J. S. RISIEN RUSSELL, M.D., M.R.C.P.—"An Experimental Investigation of Eye Movements." Journal of Physiology, Vol. 17, 1894.

J. S. RISIEN RUSSELL, M.D., M.R.C.P.—"Further Researches in Eye Movements." Journal of Physiology, Vol. 17, 1894.

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BACTERIOLOGY.

R. W. BOYCE, M.D., and NUSSERWANJI SURVEYOR, M.D.—"On the Fungus-Foot Disease of India." Brit. Med. Journal, September 22nd, 1894.

REPORT.

The work of the Pathological Department has been actively pursued during the past year.

TEACHING.

On the appointment of Dr. Boyce to the Holt Professorship of Pathology established in University College, Liverpool (as recorded in the Fourth Volume of these Reports), Dr. Bulloch was appointed Assistant to the Department, and carried out the teaching in the classes of Morbid Anatomy and Bacteriology. On the termination of his period of office Dr. A. H. White was appointed to the vacancy.

The teaching in the Chemical Department is still greatly hampered by want of proper or adequate accommodation. The former Bandaging Room has been allotted to this purpose, but although the efficiency of the class-work has been seriously impaired by restriction of space, it is hoped that the adaptation of the additional room to its new purpose will be completed during the coming vacation.

RESEARCH WORK.

I.—General Pathology.

The facilities for original investigation have been added to by the purchase of a large Smith's Chronograph, and of a $2\frac{1}{2}$-horse power Electromotor. The purpose of the latter is to afford driving power for recording, artificial respiration, and centrifugal apparatus.

The following gentlemen have worked in the Laboratory since the publication of the last Report.

Dr. Loewenthal has commenced a research into the phenomena of fatigue of the cortex cerebri, and on the question of the commissural relations of cortical centres of true bilateral representation.

Mr. Marshall has finished the first part of his observations on the path of the epileptic discharge, including chiefly the effects of hemisection in the spinal cord in the cat. This will shortly be published by the Royal Society.

Dr. May has resumed his investigations into segmental representation of movement existing in the spinal cord.

Dr. Mellus has completed an elaborate research into the anatomical position of the pyramidal fibres degenerating sequentially to the removal of restricted portions of the cortex cerebri. The full paper will be published by the Royal Society.

Dr. Risien Russell's investigations in connection with the functions of the cerebellum formed the subject of a paper which was published in the Philosophical Transactions of the Royal Society, and which, together with a paper on the brachial plexus of the dog, also published in the Transactions, was included in the last volume of papers issued from this Laboratory. His paper dealing with the connections of the cerebellum, as proved by tracing the paths which degenerate after ablation of parts of the organ, will appear in the Transactions of the Royal Society, and an abstract of the paper is included in the present volume.

The work upon the influence of the cerebrum and cerebellum on eye movements, which was in progress when the last Report was issued, has been completed, and the results are embodied in two papers published in the "Journal of Physiology," both of which will

be found in the present Report. The case of defective development of the central nervous system in a cat, investigated by him, was published in "Brain," and is also to be found in the present volume.

Dr. Russell has since investigated the condition of the central nervous system of a puppy, with symptoms pointing to defect of the cerebellum during life, in which the changes, though extensive, were limited to the cortex of the cerebellum, the corpus dentatum being intact. The case was the subject of a paper read before the last meeting of the Neurological Society, and will be published in "Brain."

The same investigator has completed a research dealing with the influence of the cerebral cortex on the movements of the vocal cords, the results of which investigation were brought before the last meeting of the Royal Society. He is further engaged, in conjunction with Mr. W. G. Spencer, in an experimental investigation with regard to the correlation of the respiratory and laryngeal central nervous mechanisms.

Dr. Russell is also observing the effects of section of the individual cerebellar peduncles, and contrasting the effects of section of the inferior peduncle just as it enters the cerebellum, with the effects of section of it in the medulla; and is tracing the paths which degenerate after such lesions. He is now in a position to continue his researches in connection with red, white, and degenerated muscle, and is preparing to advance this work.

A case of acute degenerative changes in the brain of a young child has been very fully investigated by him, and will be published before long, in conjunction with Dr. Kingdon, who is responsible for the clinical observation of the case.

Mr. Walter Spencer gave in March the Arris and Gale Lecture at the College of Surgeons, "On the Central Nervous Mechanism of the Respiration" (*vide* "Lancet," 1895. Vol. I.), in which a summary of the work done during the past four years was included. He has made a series of experiments upon the vagas nerves, especially upon the intracranial roots, which will shortly be ready for publication.

Dr. Risien Russell and Mr. Spencer are now engaged on some experiments comparing and distinguishing the effects of cortical stimulation upon the respiration and larynx respectively. Some new results have been obtained, whilst the previous observations made by these two observers separately have been amply confirmed.

Dr. Stoddart is completing a large series of experiments on the conduction of efferent impulses in the pyramidal tract, with special reference to the degree of crossing of the bulbar decussation. The results so far have been very distinctive, and it is hoped will elucidate the function of the direct pyramidal tract.

Dr. Thompson is investigating certain pathological alterations in the circulation within the eyeballs.

Mr. Horsley has continued the investigation into the effects of high velocity projectiles commenced by Dr. Kramer and himself. The first part is about to be published in the Pathological Transactions of the Royal Society.

Mr. Horsley has also continued the investigation commenced by Dr. Harris and himself on Ehrlich's method of tracing oxydation processes in the living body by the metryline blue method, and the preliminary results obtained are published in the Reports of the Scientific Grants Committee of the British Medical Association, 1895.

II.—Chemical Pathology and Metabolism.

In the Department of Chemical Pathology under the guidance of Dr. Vaughan Harley :—

Dr. Nusserwanji Surveyor has completed his research on the value of β. Napthol and Bismuth Subnitrate as an intestinal disinfectant. He finds that β. Napthol causes an increase in the aromatic sulphates in the urine in consequence of its being partly absorbed and excreted as such in the urine. It has, however, an antiseptic action, which extends along the whole length of the alimentary tract, as indicated by counting colonies from the various parts after juding with it.

Bismuth subnitrate somewhat decreases the aromatic sulphates, but its action in this direction is masked by its constipating

tendencies. In counting colonies its action as a disinfectant is seen to be chiefly in the upper part of the alimentary tract. The results are shortly to be published, and an abstract given at the meeting of the British Medical Association in August, 1895.

Dr. Nusserwanji Surveyor is further carrying on an investigation in the pharmacology of anarcotine. He is investigating its action, if any, on metabolism and of its soluble hydrochlorate on blood pressure and respiratory exchange.

Dr. Goodbody is carrying on a research into the pathology of uric acid. His preliminary results on the action of piperazine on the solubility of quadriuretis are to be communicated at the British Medical Association in August, 1895. The continuation of the investigation is intended to elucidate the formation of uric acid in the organism and its relation to artificially produced gout.

Dr. Goodbody is still further analysing the sputum of pneumonia in the different stages of the disease as to its composition in proteids, fats, cholesterin, soaps, and inorganic ash.

Dr. Barratt has commenced a series of experiments on the pathological variations in the amount of sweat in such conditions as erythema, etc. He is also carrying on a research into the transudation of fluid through the skin of the frog, in the hope of elucidating some of the elements of difficulty in understanding the function of perspiration.

Dr. Dudley Cooper is continuing his investigations into the changes which occur in metabolism of general paralysis of the insane. A short report of the results so far obtained is given in the Scientific Grants Report of the British Medical Association.

Dr. H. Smith's research into the chemical composition of various pathological fluids is at present in abeyance, owing to pressure of other work. The results so far obtained are reported in Scientific Grants Report of the British Medical Association.

Dr. Lewis is at present engaged in an investigation into the metabolism and effects of diet in acute Bright's disease.

Professor Thompson and Dr. Vaughan Harley are still engaged in a research on the influence of various nerve lesions on the respiratory gaseous exchange from the lungs and blood.

Dr. Arthur White is continuing his researches in regard to the effect of repeated hæmorrhages on the chemical composition of the blood. For that part of the work referred to in Vol. III. of the Laboratory Reports Mr. White divided (with Dr. Dixon) the "Reuben Harvey Memorial Prize" (Dublin) of 1894. An abstract of results appears in the Reports to the Research Grants Committee of the British Medical Association, and the full paper will shortly be published.

Dr. Vaughan Harley has completed his preliminary investigation into the normal absorption of milk fat, and the effect of extirpation of the pancreas upon its absorption. The results obtained will be found in this volume.

He is now investigating the chemical changes milk fat undergoes in its passage along the alimentary tract, in cases in which either the pancreatic or biliary secretions are absent. This is with special reference to the importance of fat splitting and saponification in the absorption of neutral fat.

At the same time a research is in progress into the digestive and absorptive powers of the large intestine in cases when it is impossible to feed by the mouth. In connection with the latter research he is investigating the metabolism of dogs in which the large intestine has been isolated (the small intestine being connected with the rectum) from the alimentary tract. One dog in this research has not only survived the operation over a year, but has during that time gained flesh, and is in apparently very good health.

Dr. Vaughan Harley has just completed a research into the metabolism of a boy, in which the pancreatic duct was apparently obstructed. He communicated the results at the Pathological Society in May last, and the full paper is now being published in the "Journal of Pathology and Bacteriology."

III.—Bacteriology.

Dr. Smith is pursuing his investigations in connection with the antitoxin treatment of diphtheria; while Dr. R. J. Carter is working at the bacteriology of certain skin diseases.

[*From the* PROCEEDINGS OF THE ROYAL SOCIETY, Vol. 58.]

A Research into the Elasticity of the Living Brain and the Conditions governing the Recovery of the Brain after Compression for short Periods."*

By A. G. LEVY, M.B. (London). Communicated by Professor V. HORSLEY F.R.S. Received February 21,—Read March 15, 1894.

(From the Laboratory of the Pathological Department of University College, London.)

A. *Object and Method of the Research.*

1. *Introduction.*—This piece of work was undertaken at the suggestion of Professor V. Horsley, who devised the apparatus employed, and to whom I am indebted for advice and suggestions.

In view of the great frequency of compression of the brain as a pathological condition, it seems very advisable to attempt to obtain knowledge of some of the elementary factors conditioning the physical changes in the brain substance due to mechanical pressure.

The general plan adopted was (*a*) to compress the living brain (*i.e.*, the brain substance plus lymph and circulating blood) by a given weight for a given time, to measure the amount of direct compression, and, after removal of the pressure, to measure the elastic recoil; (*b*) to investigate the influence upon the recoil of varying conditions of the vascular and respiratory systems.

Finding in an early stage of the investigation that the elasticity of the brain is very far from being perfect, I was further led to investigate the conditions, vascular, &c., which favoured more complete recovery of the brain surface to its normal level, especially after periods of prolonged compression.

The following, therefore, are records of an investigation of the

* Towards the expenses of this research a grant was made by the British Medical Association on the recommendation of the Scientific Grants Committee of the Association.

physical properties of the brain substance, and deductions drawn from my observations must not be immediately applied to explain the changes in the brain seen in cases of meningeal hæmorrhage, tumours, &c., because, in order to ascertain the fundamental facts, the experiments in the present case have of necessity been made with the cranial cavity open, the dura mater partially reflected, and a certain quantity of the cerebro-spinal fluid consequently drained away. In pathological conditions the pressure is exerted in a closed, fluid-containing cavity, and hence any local compression must evoke a reaction from all parts of the cerebral environments, and all parts of the intracranial contents are at an equally exaggerated pressure. In my experiments, the cranial cavity being opened, the influence of the cranial walls is limited, and the pressure is directly exerted upon, and principally confined to, the part of the surface compressed and the mass below it.

I may mention that I started with the generally accepted premise that the elasticity of the brain is more or less proportional to the central blood pressure, and many of my earlier experiments were performed with the object of testing what at first sight seems an exceedingly reasonable view.

2. *Historical Introduction.*—I have throughout my experiments taken as an indisputable fact what was demonstrated by Grashey,* viz., that the cerebral tissue itself is practically incompressible (in fact, its coefficient of compressibility being rather less than that of water), and that any reduction in volume of the living brain must therefore be due to the squeezing out from its blood vessels, lymphatics, and ventricles, of blood, lymph, and cerebro-spinal fluid.

Grashey's experiments consisted of a careful estimation of the compressibility of the dead brain by hydraulic pressure in a delicate piezometer. His experiments conclusively showed what had indeed been the general teaching, but he was led to make this demonstration by reason of the extraordinary assertion of Adamkiewicz† that the brain tissue itself bears the brunt of the diminution of the intracranial space.

The records on compression of the brain substance are numerous, and the methods employed by the investigators (Cooper, Duret, Kahler, Pick, Leyden, Adamkiewicz, Spencer and Horsley, Dean, Hill, &c.) are very various; but these experiments have been arranged from the clinical point of view, *i.e.*, the effect of compression upon the functional activity of the nerve centres.

Some observers have noted the structural changes produced; thus,

* Grashey, "Ueber Hirndruck und Hirncompression," 'Allg. Ztschr. f. Psychiat.,' Berlin, 1887, 43.

† Adamkiewicz, "Die Lehre von Hirndruck und die Pathologie der Hirncompression," 'Sitzungsberichte d. K. Akademie, Wien,' Band 88, 1883.

Adamkiewicz investigated the structures microscopically, and Dean* by quantitative analysis, with special reference to œdema.

I can find, however, no systematic investigation into the immediate recovery of the brain after compression. Dean, in the course of his experiments, gave attention to the recovery after the compression by glass discs, but his observations were made by the unaided eye. Further, the majority of his experiments, in which the brain was examined several days after compression was removed, when secondary changes had taken place, fall into another category than those which I have carried out, for in no case were my observations prolonged for more than an hour after compression, and usually the period was much shorter. Moreover, contrary to the methods adopted by the just named observers, the influence of the cerebro-spinal fluid in the present research was excluded; the dura mater being opened, the fluid is released from all tension, and some of it escapes during the procedure described below, my object being to investigate the change in the brain mass alone.

3. *Description of the Apparatus for Measuring the Compression and Recovery therefrom.*—An apparatus was designed for the purpose of applying known weights vertically to the brain surface, so that the amount of depression of the surface could be accurately measured, and also the recoil after the removal of the weight.

This apparatus is shown in front and back view in figs. 1 and 2. It consists essentially of two supports for screwing into the skull, a plunger through the medium of which to apply the weights, and a dial to indicate the excursion of the plunger.

To consider the parts in detail: the supporting pillars consist of three portions, see fig. 1 (*a*, *b*, and *c*). The foot (*a*) screws into the bone, and (*b*) is a cap which screws on to it. The two when fitted together form a socket to receive the globular end of (*c*) the pillar, which thus acts in a ball-and-socket joint, and can be firmly fixed in any position by screwing down (*b*). By this means the pillar may be made to assume a perpendicular position when the screw has to be inserted into a portion of the skull which is not horizontal.

The pillars support the dial through the medium of the slots (*d*, *d*), and are fixed by screws (*e*, *e*), the slots themselves being firmly fixed in position by the thumb screws (*f*, *f*). These slots allow, among other movements, of lateral shifting of the dial. These arrangements conveniently give great range of movement of the dial, so that the plunger may be placed into a position of accurate perpendicularity.

The plunger consists of a straight rod, carrying above a weight pan (*g*), and, passing through the body of the dial, it has attached to it by a special arrangement a thread which, looping round the axis

* H. P. Dean, "Cerebro-spinal Pressure," 'Journal of Pathology and Bacteriology,' 1892.

Fig. 1.

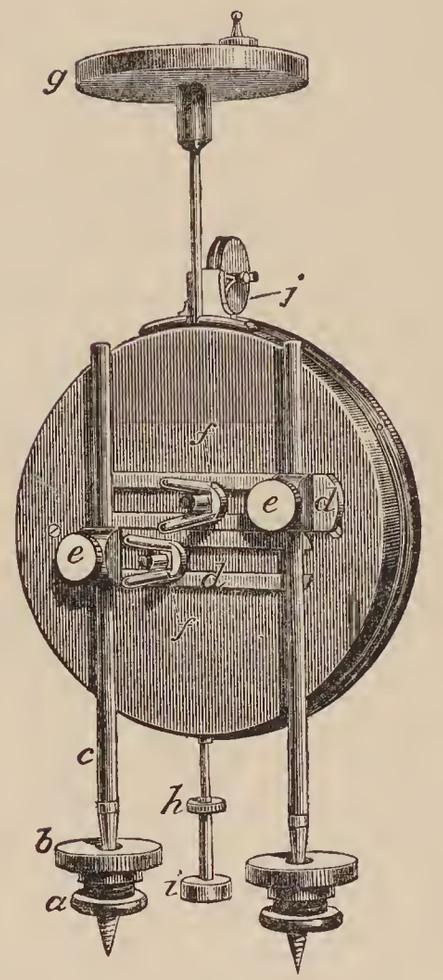
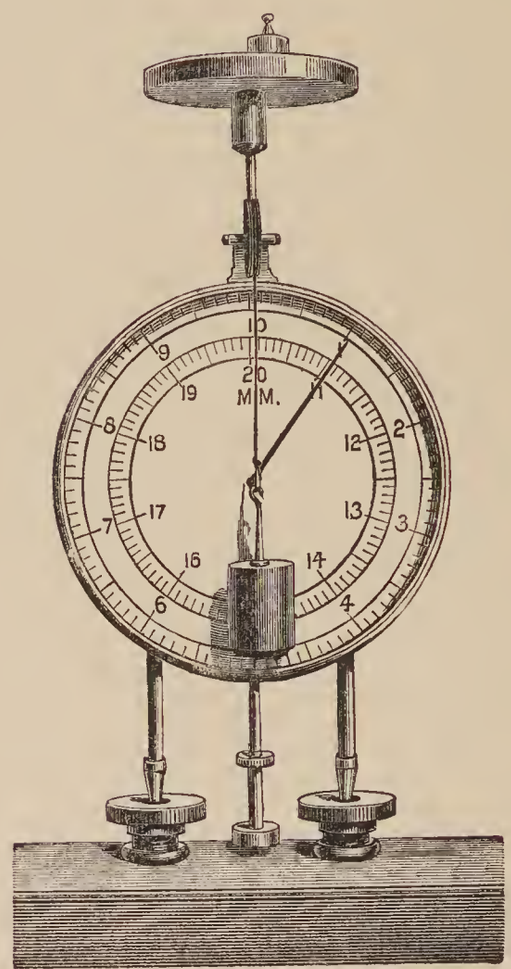


Fig 2.



of the dial, rotates this in its excursions up and down. An index hand attached to the axis indicates tenths of millimetres on the dial.

Below, the plunger has screw arrangements (*h*), by which discs (*i*) of varying sizes can be applied. In all experiments a disc of 1 cm. diameter was used unless otherwise mentioned, and it was by the screw attachment correctly adjusted to the surface of the brain. The weight of the plunger was accurately counterbalanced by a weight which acts over a pulley (*j*), so that the disc remains at rest in any position, *e.g.*, on the brain surface, without exerting any pressure when there is no weight in the pan.

This suspended counterbalancing weight also acted as a plumb line by which the perpendicularity of the plunger was secured, this position being essential to avoid all friction. The figures show the apparatus applied to a horizontal surface.

4. *Method of Experiment.*—The animal, invariably a dog, was kept under ether through the medium of a glass cannula, inserted into the trachea and attached by india-rubber tubing to a funnel, this latter being placed over cotton-wool saturated with ether. The narcosis must be maintained equably throughout the experiment, to avoid irregularity in respiratory movements. The head was firmly sup-

ported in the usual holder. The skull was exposed on one side, and the median and fronto-temporal ridges chiselled away as far as necessary, so as to give a flat surface for inserting the screws. The skull was trephined close to, but carefully avoiding, the longitudinal sinus. I found hæmorrhage a very troublesome accident, and that it was essential to stop it by means of wax and amadou before proceeding with the experiment, as the presence of even a thin layer of blood on the cortex marred the result. The object of applying the compression as near as possible to the middle line was to arrange the line of pressure perpendicularly downwards, so as to avoid any elastic reaction from the falx cerebri; this seemed to be more important in using large weights, which evoke larger excursions. I enlarged the opening in the skull with bone forceps, so as to allow of easy insertion of the plunger, and give sufficient margin to observe the condition of the brain surface. The next step was to reflect the dura mater, insert the screws (using a guarded bradawl to make preliminary holes), and then to erect the apparatus so that the disc of the plunger rested flat on the surface of the brain, and the plunger itself was absolutely perpendicular.

The blood pressure was recorded by means of a mercurial manometer connected with the femoral artery. The respirations were traced by means of a Paul Bert receiver and a Marey recording tambour.

In performing an experiment I noted the moment of applying the weight to the pan, and then recorded the figures the index pointed to at intervals of so many seconds during and after compression, and also read off the blood pressure at stated intervals.

5. *Considerations Affecting the Plan of Experiments.*—A few remarks on special conditions observed during my experiments may now be briefly noted.

(*a.*) Various conditions of the cranium and its contents, affecting the apparent elasticity of the brain, and requiring attention, are as follows:—

Adhesions of the pia mater to the dura mater, as, for instance, by vessels running from one to the other.

The Falx Cerebri.—This is not large as a rule in the dog, often not more than 5 or 6 mm. broad in a small dog, and is not likely to have much influence, but large weights applied in a direction fairly perpendicularly to its surface might reasonably be expected to be limited in effect by its elasticity.

The Tentorium.—This is generally almost totally ossified in dogs, but in some dogs there exists sufficient membrane to prove a factor in causing some elastic reaction from the base of the skull.

The Shape of the Cranium.—It seems probable that the vertical depth of the skull cavity should modify results somewhat, as with a

deep skull a greater depth of brain substance comes directly under compression than in the case of a flat skull, but this and the foregoing conditions have but a subsidiary influence upon the effects observed, the main factor which influences the more immediate recoil of the brain surface, in experiments performed upon the organ *in situ*, being the rigidity of the bony floor it rests upon.

(*b.*) Moulding.—After a compression of thirty seconds or so there frequently results a faint ringed impression of the disc—this usually disappearing in about half an hour. After several experiments have been performed upon the same spot, a considerable saucer-like depression in some cases ensues.

(*c.*) Œdema.—On several occasions a curious phenomenon was observed, which most probably has its origin in local œdema. It is more especially marked in experimenting with small weights, 20 to 50 grams, applied for a couple of seconds only. When the weight, after compression, has been removed, and the brain surface, in recovering, has ceased to push the disc up farther, then if the passively resting disc be removed from the surface, the latter will start a further rise almost immediately, so that in a few minutes it may even be at a higher level than that at which it stood when the experiment was started. After more severe compression this is not observed.

(*d.*) Powerful respiratory movements, as will be shown directly, are liable to vitiate results by aiding recovery after compression, through the medium of increased venous pressure. Hence the necessity already mentioned of maintaining a fairly deep narcosis.

(*e.*) The direct effect of compression upon the blood pressure and respiration.

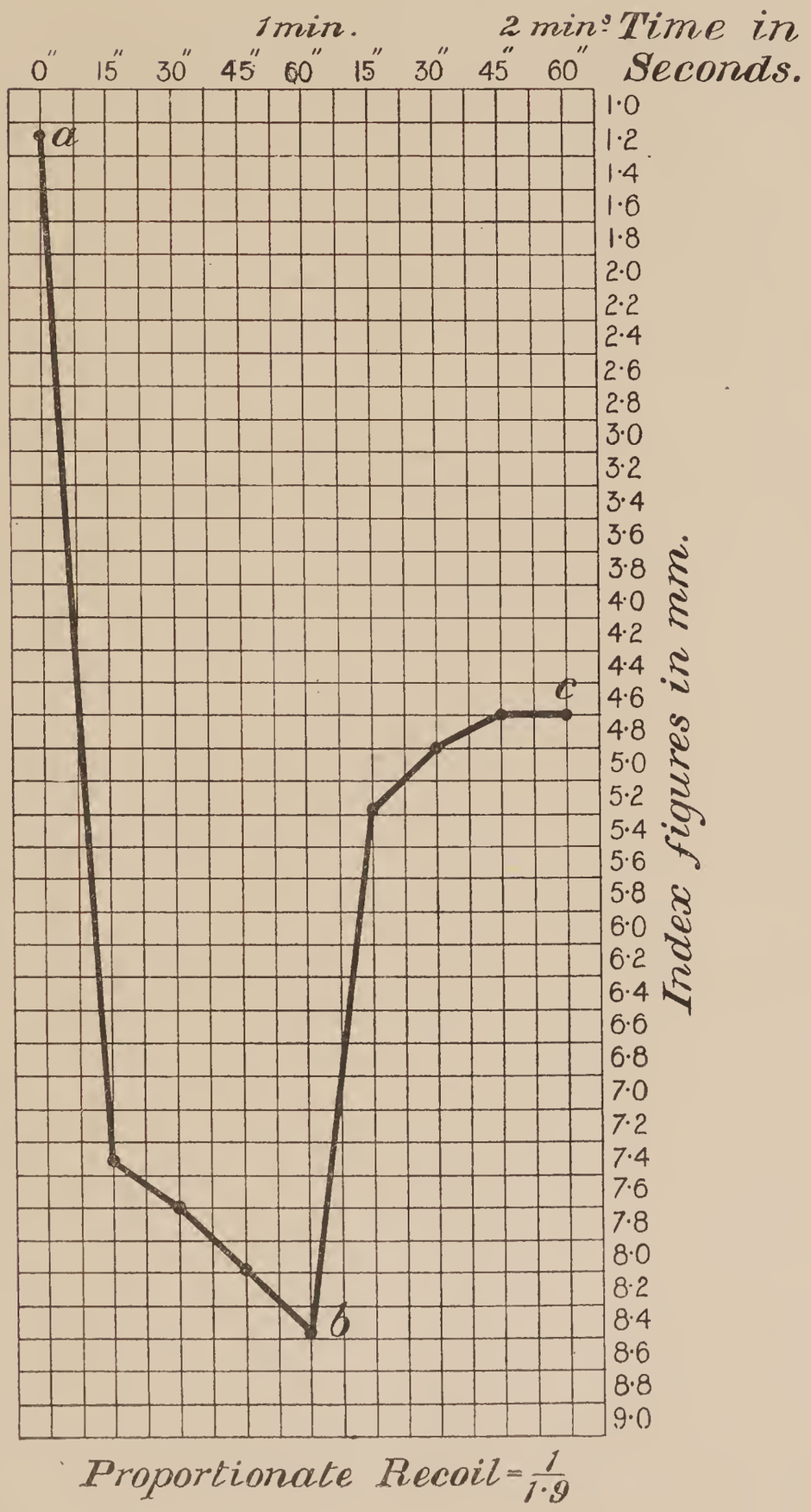
I found that the local compression by any weights that I employed was, in view of the cranium being freely opened, insufficient to produce any effect, either upon the blood pressure or respiration, this being so far fortunate as then could be no indirect influence from this cause upon the elasticity of the brain. The minimum weight which can affect respiration, even slightly, was 200 grams.

B. *Results of Compression Experiments on the uninjured Brain, the Blood Pressure being normal.*

(*a.*) *Definitions.*—I employ the term "uninjured brain" to denote that no previous experiment has been performed on the same brain; the effect of previous compression in destroying the value of subsequent experiments is discussed later.

The term "excursion" I have applied to the extent to which the plunger enters into the cranial cavity (by a reason of sinking of the brain) on a weight being applied. Fig. 3 (*ab*).

Fig. 3.



By the term "recoil" I mean the amount of recovery of the brain as measured by the instrument. Fig. 3 (*bc*).

(*b.*) *Results of the Experiments.*—In this section, unless otherwise stated, the weight used was 50 grams and the compressing disc 1 cm. in diameter.

i. *Excursion.*—The character of the excursion evoked by a compression of 50 grams for one minute is as follows :—

Firstly, there is a rapid fall of the index in the first few seconds; this being followed by a very much more gradual compression (fig. 3). So that three-fourths of the whole excursion may take place in the first two seconds.

The absolute extent of the excursion varies in different dogs very considerably (the time of compression being equal); thus the amount in one minute varied in two separate cases from 4·5 mm. to 7·3 mm. Variation in the absolute amount of depression of the brain surface is to be expected where differently shaped heads were experimented upon.

There appeared to be some relation between the size of the dog and the extent of the excursion, probably because there is in a large brain a greater depth of collapsible mass beneath the plunger. On the other hand, it was very noticeable that the extent bears no relation to the height of the blood pressure; in fact, it is curious that often the largest excursions accompanied a normally high blood pressure (*i.e.*, a well-filled, highly collapsible brain).

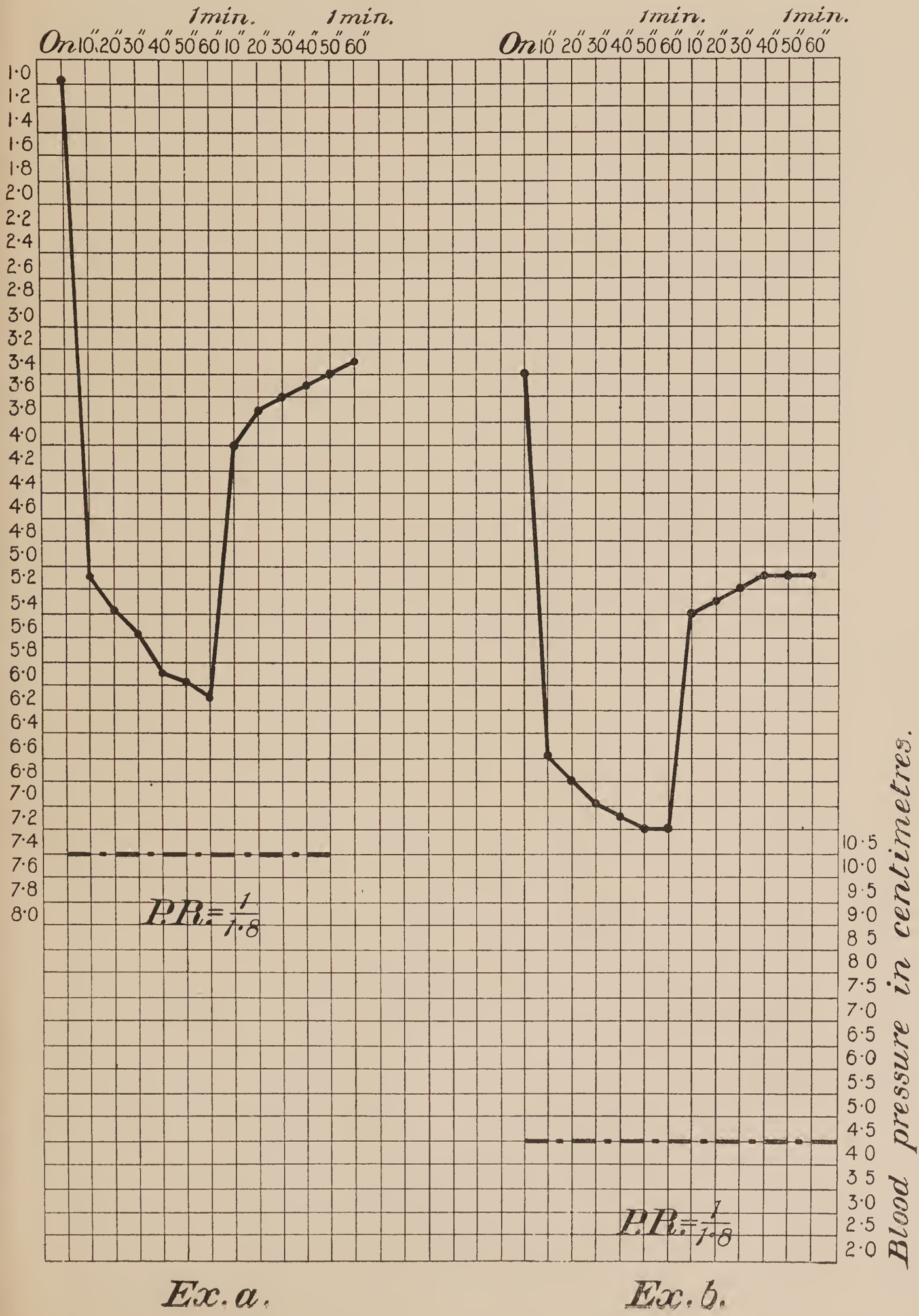
Observations were also made with a very short time of compression, such as of two seconds' duration. Under these circumstances the absolute excursion is notably less, viz., 2·4 to 3·5 mm. I have already mentioned the rapidity of the development of the first part of such a curve. The actual curve is shown in fig. 5.

ii. *Recoil.*—The character of the recoil after one minute compression with 50 grams is well shown in fig. 3. As a rule it is nearly completed in a few seconds, but develops further during one to two minutes, and then usually stops. After this point the process undoubtedly continues in many cases, but it is too gradual to record. After half to three-quarters of an hour, the brain in most cases will be found to have resumed its normal level. The recoil was measured at the point at which it became apparently stationary.

For convenience of expression, to denote the relation of the recoil to the compression, I employ a fraction, the numerator of which is the numerical value of the recoil expressed as unity, and the denominator is the value of the excursion compared to the recoil. Thus, where the excursion is twice the recoil the fraction = 1/2; and to the ratio I apply the term "proportionate recoil." The *smaller* the fraction the *less* the elasticity; the nearer it approaches unity the more perfect the elasticity.

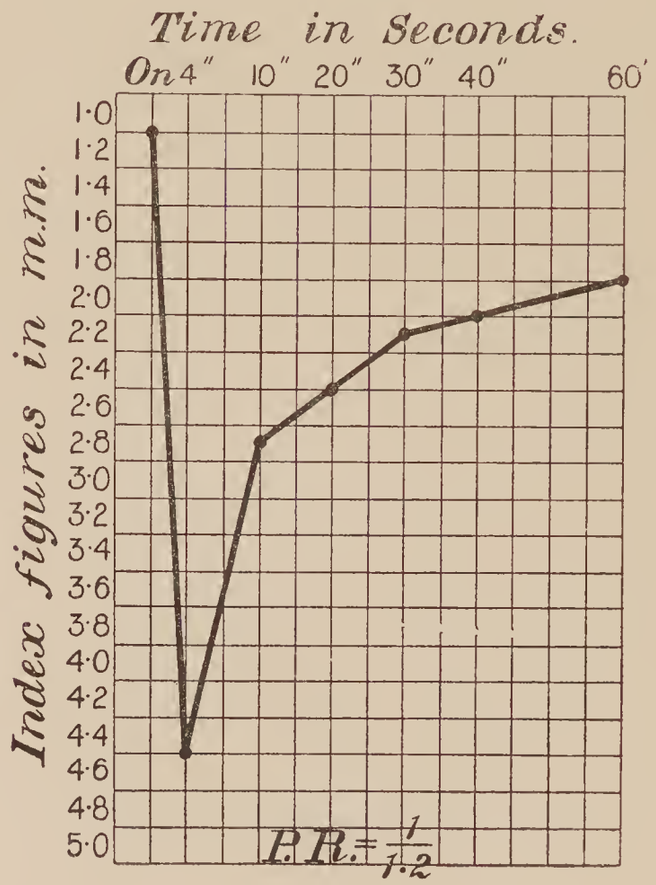
We are now in a position to see the degree to which the brain recovers itself after a compression of 50 grams for one minute. The proportionate recoil is very constant, *i.e.*, nearly 1/2, in many cases almost exactly so, but varying within the extreme limits of 1/1·8 to 1/2·3 (*e.g.*, fig. 3 = 1/1·9, fig. 4 = 1/1·8).

FIG. 4.


1 min.
1 min.
On 10″ 20″ 30″ 40″ 50″ 60″ 10″ 20″ 30″ 40″ 50″ 60″
On 10″ 20″ 30″ 40″ 50″ 60″ 10″ 20″ 30″ 40″ 50″ 60″
1·0 1·2 1·4 1·6 1·8 2·0 2·2 2·4 2·6 2·8 3·0 3·2 3·4 3·6 3·8 4·0 4·2 4·4 4·6 4·8 5·0 5·2 5·4 5·6 5·8 6·0 6·2 6·4 6·6 6·8 7·0 7·2 7·4 7·6 7·8 8·0
Index figures are millimetres.
P.R. = 1/1·8
P.R. = 1/1·8
10·5 10·0 9·5 9·0 8 5 8 0 7·5 7·0 6·5 6·0 5·5 5·0 4·5 4 0 3 5 3·0 2·5 2·0
Blood pressure in centimetres.
Ex. a.
Ex. b.

If, however, the pressure be kept up for only two to five seconds the recoil is more perfect. In fact, the immediate recoil which takes place in the first two or three seconds may give a ratio of 1/2 or even 1/1·5; after an interval of thirty seconds or so it may be 1/1·4 or even nearly 1. *E.g.*, Experiment 12*a* = 1/1·2 (fig. 5), Experiment 14*a* = 1/1·5 (immediate).

Fig. 5.



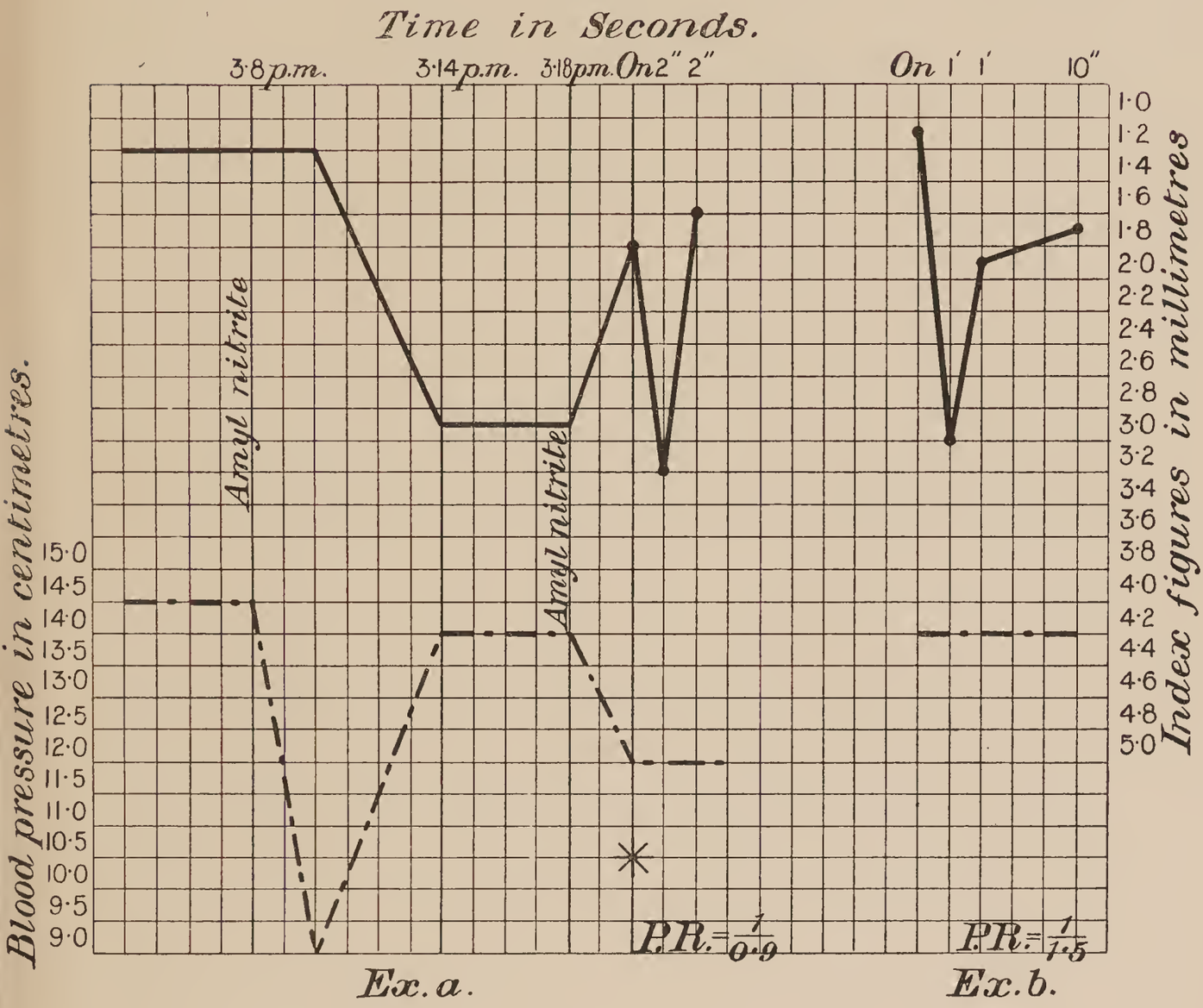
If the pressure be prolonged, say, for six minutes, the fraction becomes smaller, and this is shown in fig. 6, where the ratio = 1/2·74, and the surface does not further recover after a long interval—more than half an hour.

Thus we see that although the elastic reaction of the brain is very fair when the compression lasts only a few seconds, longer compression affects the brain in such a fashion that it does not recover so readily.

Thus, also, we see that for the same weight and same length of compression, the elasticity is very much the same in different brains; *i.e.*, with a large excursion there is a proportionately large recoil, and *vice versâ*.

iii. *Results of Experiments with varying Weights.*—A few experiments performed with a weight of 20 grams show a comparatively small excursion, but the ratio is similar to that obtained with a 50 grams weight. Weights such as 100 grams and over seem to be

FIG. 6.



somewhat prejudicial to a good reaction; they produce a somewhat larger excursion. [A weight of 200 grams will gradually lacerate a dead brain.]

C. *Consideration of the Relation of the foregoing results to the Blood Pressure.*

We may first take in this connexion the experiments in the series just described, and compare the reaction to the height of the blood pressure, to test the influence of the latter as a possible factor in the establishment of the recoil of the brain.

(*a.*) *Comparison of Experiments on the uninjured Brain in different Dogs with individually different, but normal, Blood Pressures.*—Below is a table of experiments performed on the normal brain in the course of which the blood pressure was measured.

It will be seen that there is absolutely no relation to be found between the individual "elasticities" and blood pressures.

Experiment.	Time of Compression.	Proportionate recoil.	B. P.
4*a*	1 minute	1/1·8	125 mm.
6*a*	1 „	1/1·8	105 „
7*a*	30 seconds	1/1·9	110 „
8*a*	30 „	1/2·2	150 „
9*a*	30 „	1/2	105 „
12*a*	4 „	1/1·2	140 „
14*a*	2 „	1/1·14	125 „
20*a*	2 „	1/2	120 „

The most noticeable of these is Experiment 8*a*, in which, although the pressure was comparatively very high, the reaction was almost at its minimum.

It is clear, then, that the recovery of the volume of the brain is not due to the pressure at which it is irrigated with blood.

Though these facts appeared to be thoroughly demonstrative, I established a number of control observations to further test the question.

The first method which suggested itself was naturally that of lowering the blood pressure very markedly by bleeding. This procedure, however, of necessity involves the measurement of the recoil of the brain thus rendered anæmic being taken from a preparation which had already been compressed once; this, of course, introduces an error, and hence the further question has to be considered how far does one compression experiment have an influence on a consecutive one.

When compression has lasted for thirty seconds or more it is obviously necessary to allow a sufficient interval to elapse to allow the damaged brain fairly to recover—such an interval as half to three-quarters of an hour, sometimes more; that is to say, I waited till the surface had regained its normal level. Sometimes it is impossible to wait for complete recovery, and, of course, in such a case an element of error is introduced; but when the time of compression is short, ten minutes is quite enough to allow so as to avoid any appreciable vitiation, of which fact I have satisfied myself experimentally.

(*b.*) *Comparison of Experiments performed on the same Brain before and after lowering the Blood Pressure by bleeding.*—After an experiment, conducted as above described at normal blood pressure, I bled the animal from the carotid artery.

As a rule, a large loss may occur without much fall of pressure, and the fall, when it does occur, takes place very suddenly. If the splanchnics be previously divided, the fall takes place earlier and more regularly. Usually I bled to the extent of 150 to 300 c.c.

By this means there could be produced an enormous fall of blood pressure, sometimes as much as 100 mm. (*e.g.*, from a normal pres-

sure of 125 mm. down to one of 20 mm.). But, under these circumstances, the fall is due to a draining of blood from all parts of the body, the brain included, and hence the latter begins to collapse soon after the bleeding has been started. This collapse, however, is not always great. Thus, in one experiment (fig. 4), after allowing the brain to recover from the trial experiment, and then bleeding 150 c.c., the fall of blood pressure of 60 mm. thus produced only caused the brain to collapse so that its vertical thickness was reduced by not more than 2·4 mm.

Of course, this collapse produces a new set of intracranial conditions, *e.g.*, the brain contains less fluid, and hence its *texture* is altered; it does not fit its surroundings so closely—its vertical depth is less. These new conditions act in diverse ways as regards its elasticity.

But we cannot disregard the fact that the fall of blood pressure measured in the femoral artery is very great, and, were there any measurable direct relation between the elastic reaction and the blood pressure, this fall, especially when the brain collapse was not great, would make itself evident in spite of the altered conditions under which the second experiment has to be performed.

The following table gives the results of experiments of this kind (p. 14).

Summary.—In Nos. 4 and 8 there is a distinct diminution in recoil. In No. 6 the recoil is exactly the same in both experiments, and these being conducted under comparatively favourable circumstances as regards the fall of brain surface, this result is of more value than the others.

In No. 7 there is an actual increase in "elasticity."

In every case the excursion is diminished after bleeding.

It will thus be seen that there is no constant relation between the fall of blood pressure and the proportionate recoil, and that in those cases in which a lowered pressure *is* accompanied by a lowered elasticity, the diminution is very small, and in no way commensurate with the fall. A series of bleeding experiments, performed without registering the exact fall of blood pressure, gave results similarly divergent.

(*c.*) *Comparison of the Results of Experiments in which the Blood Pressure was Varied by means of Amyl Nitrite.*—It was now evident that, if possible, a method should be found of reducing or raising the central arterial pressure without causing an alteration in the level of the brain surface. In order to do this, the blood supply to the brain must be kept up or diminished according as the central blood pressure falls or rises, *i.e.*, when the pressure falls the cerebral vessels should dilate, and *vice versâ*.

Now, supposing a fall could be produced by a general vaso-motor action, brain arteries being included, here we should have the condi-

No. of experiment.	Normal Brain.			After Bleeding.			Remarks.
	B. P. in mm.	Proportionate recoil.	Excursion.	B. P. in mm.	Proportionate recoil.	Excursion.	
4	120	1/1·8	5·8	25	1/2	3·9	50 grams applied for 1 minute. Bleeding to the extent of 270 c.c No record of extent to which the brain surface sank.
6 (Fig. 4)	105	1/1·8	5·1	45	1/1·8	3·8	50 grams applied for 1 minute. Bled 150 c.c. Fall of brain surface = 2·4 mm.
7	120	1/2·3	5·0	30	1/2·1	2·7	50 grams applied for 30 seconds. Bled 170 c.c. Fall of brain surface = 3·8 mm.
8	150	1/2·2	5·7	62	1/2·47	3·7	50 grams applied for 30 seconds. Bled 200 c.c. Fall of brain surface = 3·5 mm.

tion required. The presence of vaso-motor fibres to the cerebral arteries has been denied, or, at any rate, they have never been demonstrated; but Roy and Sherrington* have shown that the calibre of the cerebral vessels may be altered by certain substances, notably acids and alkalies, and they consider this a direct action on the vessel walls. It occurred to me to try the effect of amyl nitrite, and I found that I could obtain a good fall of blood pressure, whilst the brain surface would remain at the normal level, or, if previously depressed, it would rise.

It is an interesting fact, and one which has a bearing on the vaso-motor question just referred to, that the subsequent recovery of blood pressure is accompanied by a *fall* of the brain surface. This is well shown in fig. 6.

It is obvious from my experiments that the brain is, under the effect of the nitrite, undoubtedly flushed with blood to an extent sufficient to neutralise its tendency to collapse; whether by vaso-motor or local action on the vessel walls it matters little, as far as the purposes of my experiment go. I see no reason to believe that the flushing is a result of increased venous pressure, this being the alternative explanation usually suggested. I administered the drug by means of clinical capsules, one or two at a time, crushed, and placed under the ether funnel. I thus obtained differences in the general blood pressure of from 20 to 30 mm. of mercury, and yet the brain surface remained at a constant, or nearly constant, level.

The chief difficulty in this method lay in the short time during which the fall lasted, thus necessitating very prompt action so as to apply the compression at the right moment.

The results of four experiments are tabulated below (p. 16).

It is seen that in each case we find that with the lowered blood pressure the elasticity is increased, markedly so in Nos. 17, 18, and 20, thus still further emphasising the fact that the elasticity does not, or at any rate *need* not, depend on central blood pressure. It is also seen in the experiments performed under the influence of the nitrite that the excursion is less. Thus, then, we find a true increase of recoil under the vascular conditions induced by this drug.

D. *Comparison of the Results of Experiments in which the Effect of Increased Venous Pressure on the Recoil of the Brain was Measured.*

(*a.*) *Anatomical Considerations.*—These experiments were undertaken in view of the marked influence which variations in venous pressure are held to exert on cerebral vascular conditions.

* Roy and Sherrington, "Regulation of the Blood Supply to the Brain," 'Journal of Physiology,' vol. 11.

No. of experiment.	Normal Brain.			During administration of Amyl Nitrite.			Remarks.
	B. P. in mm.	Proportionate recoil.	Excursion.	B. P. in mm.	Proportionate recoil.	Excursion.	
17 (Fig. 6)	140	1/1·5	1·9	120	1/0·9	1·3	20 grams applied for 2 seconds. The small excursion as a result of a light weight is noticeable. The ratio under amyl nitrite shows that the recoil is greater than the excursion. (See fig. 6.)
18	95	1/1·3	3·3	70	1/1	2·0	50 grams applied for 2 seconds.
19	105	1/1·6	3·2	90	1/1·5	3·1	50 grams for 2 seconds.
20 (Fig. 7)	120	1/1·7	3·4	90	1/1·23	3·2	50 grams for 1 second.

To render this part of the paper more comprehensible, it is necessary to give a short description of the vessels providing for the outflow of blood from the dog's skull, as their anatomy presents many points of difference from that of the human being. The details are chiefly as stated by Ellenberger and Baum.*

The greater part of the venous blood leaves the skull through the foramen magnum by route of the inferior occipital sinuses, and enters the venous plexus of the vertebral column.

The vein next in individual importance is the *superior cerebral*, which finds exit from a foramen situated, on either side, between the post-glenoid protuberance and the external auditory meatus. It communicates, through the medium of the *meatus temporalis*, with the lateral sinus of its own side. It is often of considerable size, and is one of the chief sources of the internal maxillary vein.

The internal jugular receives, along with other branches, the *inferior cerebral* vein, which runs in the carotid canal and opens into the cavernous sinus.

The internal jugular is very small, and carries away but little cerebral blood.

Running through the orbital fissures are important veins (ophthalmo-cerebral and cerebro-facial), which connect the cavernous sinuses with the external maxillary veins.

In addition to these, there are numerous emissary veins, and between all the channels of exit named there is free anastomosis.

(*b.*) *Method of Experiment.*—I exposed the accessible cranial veins, viz., the external and internal jugulars, and internal maxillaries; the latter I followed nearly to their termination in the superior cerebrals. I then blocked the various veins in succession by clamps, and performed the usual experiment upon the congested brain.

To make the experiments more complete in one case, I measured the change in the venous pressure in the lateral sinus by means of a cannula inserted into one superior cerebral vein and connected with a water manometer. Directions for dissecting out this vein are given by Gärtner and Wagner,† but I always found it necessary to remove the angle of the lower jaw in addition.

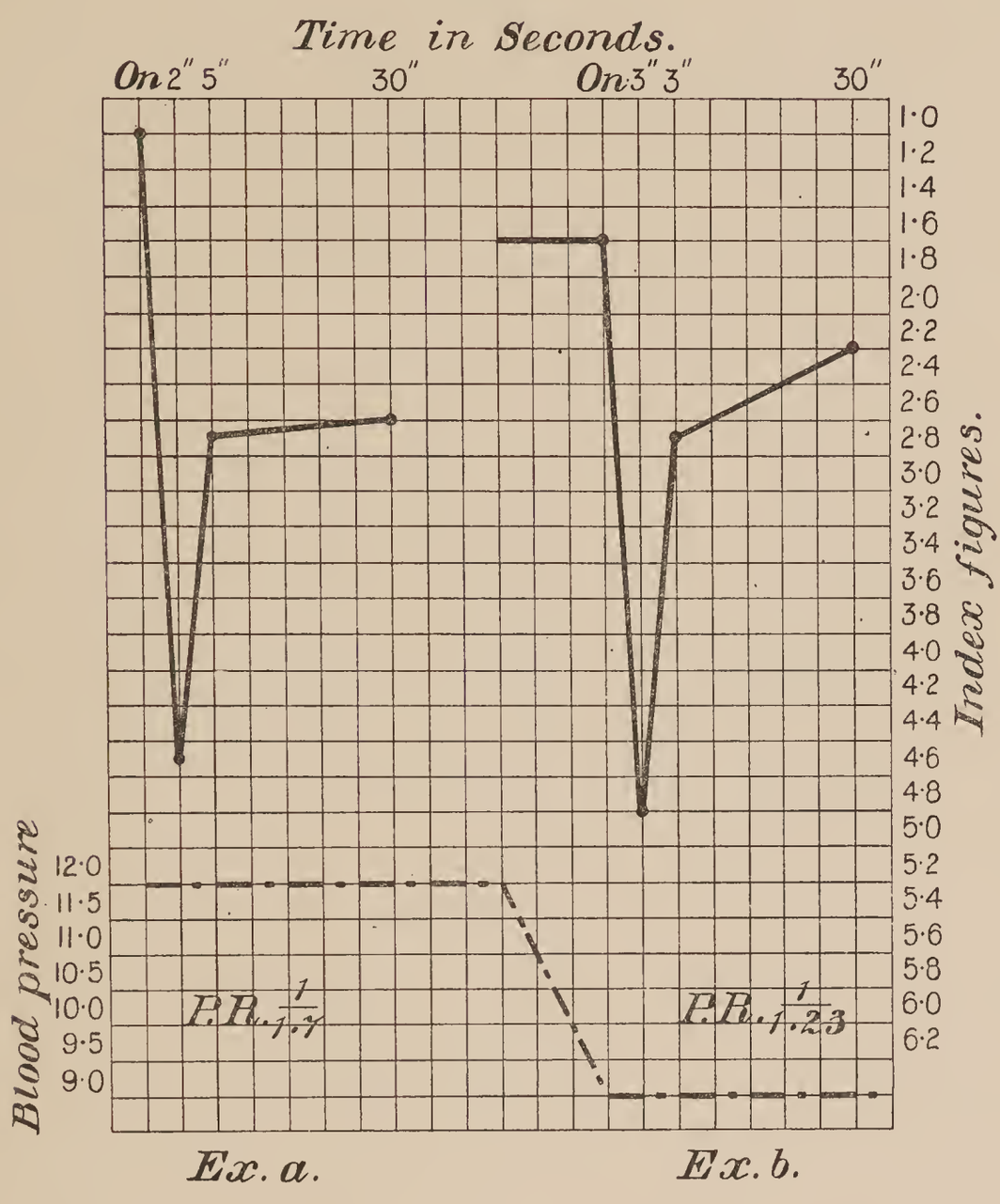
In the following table I have noted the degree of elevation of the brain surface, denoting the amount of congestion following blocking of the main venous outlets.

* 'Anatomie des Hundes.'

† Wagner and Gärtner, 'Med. Wochenschrift,' Wien, 1887, Nos. 19 and 20.

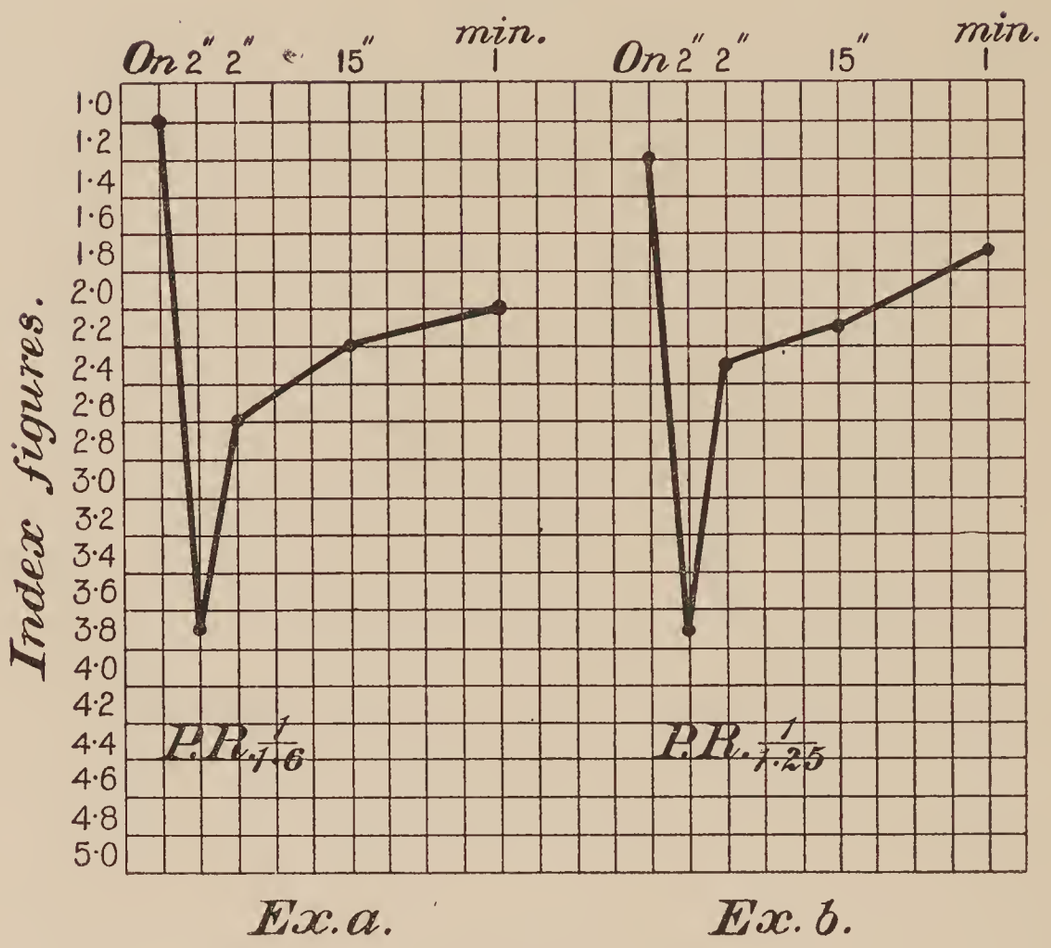
No. of experiment.	Normal Brain.		Congested Brain.			Remarks.
	Proportionate recoil.	Excursion.	Veins clamped.	Proportionate recoil.	Excursion.	
23 (Fig. 8)	1/1·6	2·7	Both superior cerebrals	1/1·25	2·5	This was an experiment in which the change in the venous pressure was directly observed; the manometer registered 6·5 cm. in one superior cerebral, and this rose to 13 cm. when the other was clamped. The increase in the immediate recoil is also noticeable. (See fig. 8.) 50 grams for 2 seconds.
25(*a*)	1/1·4	4·5	One superior cerebral	1/1·4	4·4	50 grams applied for 5 seconds.
25(*b*)	1/1·4	4·5	Both superior cerebrals	1/1·48	3·7	50 grams applied for 5 seconds.
26(*a*)	1/1·36	3·8	Both superior cerebrals	1/1·3	3·2	50 grams applied for 5 seconds.
24(*a*)	1/1·6	2·9	Both internal jugulars	1/1·6	2·8	50 grams applied 5 seconds: clamping these veins does not produce any perceptible expansion of the brain.
24(*b*) (Fig. 9)	1/1·6	2·9	Both external and internal jugulars	1/1·4	3·8	50 grams applied for 5 seconds. Surface (being previously depressed) rose 2 mm. on clamping the veins. The recoil is measured in this case at the end of 15 seconds only, the very marked recovery of the congested brain at the end of 2 minutes being shown in fig. 9.
25(*c*)	1/1·4	4·5	Both external jugulars	1/1·4	4·1	50 grams for 5 seconds. Brain surface rises 1·8 mm.
26(*b*)	1/1·36	3·8	Both external jugulars	1/1·4	3·9	Surface rises 1·6 mm. 50 grams applied for 5 seconds.

Fig. 7.



Thus we see that, out of three experiments (24*b*, 25*c*, and 26*b*) in which both external jugulars were blocked, in only one (viz., 24*b*) is there an appreciable increase in recoil. (In this case, to be sure, the internal jugulars were also included, but, in the light of experiment 24*a*, I cannot believe that these insignificant veins are a factor worth considering.) Experiments 25*a*, 25*b*, and 26*a* show no increase of elasticity on blocking one or both superior cerebrals in any one of the cases, and hence are in strong contrast to 23*a*, in which the increased recoil is quite noticeable. This last experiment is also of importance, from the fact that the rise in venous pressure accompanying the increase in elasticity was actually measured, and it shows what a very considerable rise in the pressure (double the normal in this case) is necessary to influence elasticity at all, and is an indication of how far we may disregard the effect of small changes of venous pressure as factors vitiating results set forth in former sections of this paper.

FIG. 8.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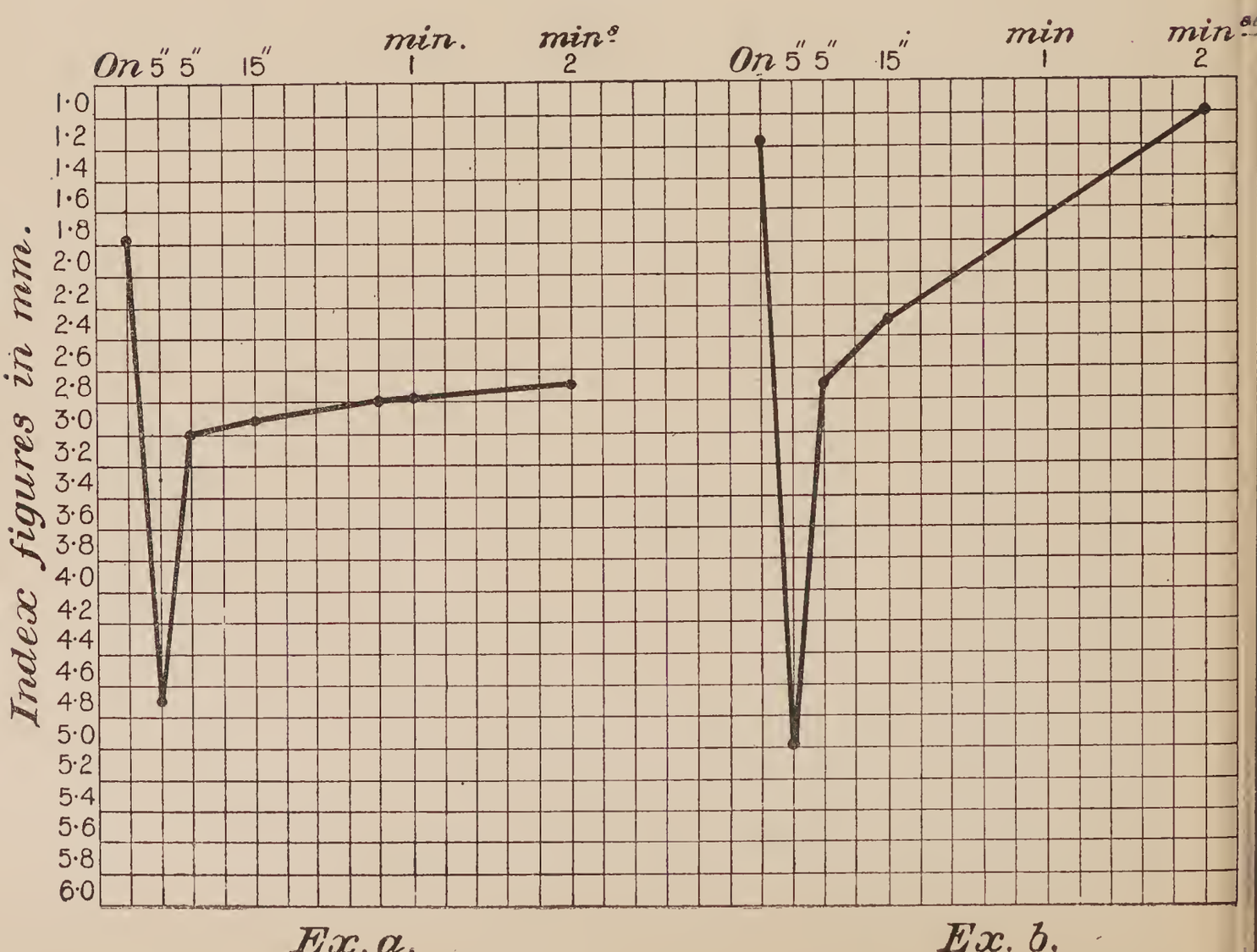
Ex. a.
Ex. b.

FIG. 9.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Ex. a.
Ex. b.

Experiments 25*c* and 26*b* show that a venous congestion of brain (as indicated by its expansion) is not necessarily accompanied by an increase of elasticity.

The failure to obtain changes in elasticity in every case must, I think, be attributed to the variation in calibre of the various channels of outflow, chiefly, probably, as regards the communications with the vertebral plexus; the common occurrence of variations in the size of the superior cerebral is patent after a few dissections.

E. *Experiments illustrating the Influence which varying Vascular Conditions have in Restoring the Volume of a Brain which has undergone Prolonged or Severe Compression.*

(*a.*) *Influence of a Rise of the General Blood Pressure.*—After the brain has been compressed as described for six minutes, the elasticity, as before mentioned, is considerably reduced, and the brain surface continues depressed for a long period. If now the etherisation be diminished, the blood pressure may be caused to rise gradually, but considerably, without anything more than a comparatively insignificant rise in the level of the brain surface accompanying it (see fig. 10, in which the blood pressure rose 35 mm. in the space of 12 minutes). Thus we find a notable difference in the reactions of normal and compressed brains to increase of blood pressure. As is well known, in the uninjured brain the surface rises and falls concurrently with variations in the blood pressure.

(*b.*) *The Influence of Venous Congestion produced by Asphyxia.*—In cases of prolonged or severe compression the brain surface may nearly always be made rapidly to recover by inducing asphyxia. In an experiment (fig. 11) the brain had been severely compressed by repeated experiments on the same spot, so that the recoil was small and had become stationary in one minute. A rise of blood pressure of 30 mm., induced by diminishing the degree of etherisation, had no appreciable effect, but total recovery rapidly supervened with the development of asphyxia. This recovery cannot be ascribed to the rise in the general blood pressure induced by the asphyxia (in this case only 10 mm., which contrasts with the 30 mm. produced by diminishing the ether supply). This is also borne out by the fact that the recovery of the surface may be obtained when there is *no* rise of the blood pressure, as sometimes occurs during asphyxia, or the expansion may actually progress whilst the blood pressure is in its stage of fall.

Frequently the surface commences to recover when the asphyxial gasps are at their strongest, but recovery will go on when the respirations are small or even when they cease, as they will sometimes, directly the trachea is clamped.

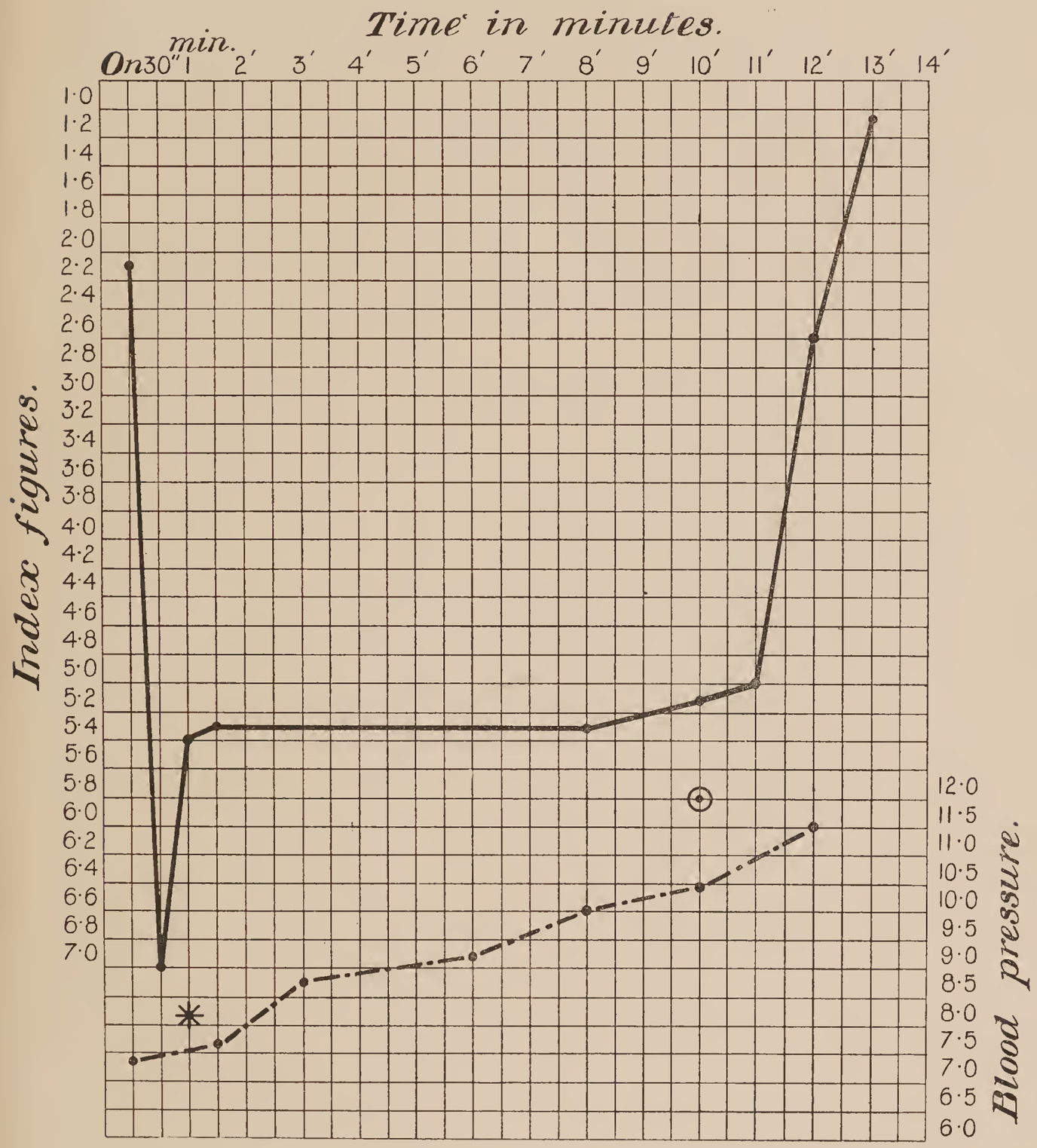
Fig. 10.

The extent of recovery varies in different cases; rarely it fails to take place at all.

It is important to notice that not only does the general surface of the hemisphere rise, but that the saucer-shaped depression due to compression is obliterated.

To obtain a definite idea of the extent to which the pressure in the cerebral veins rises during asphyxia, I took the venous pressure during asphyxia from the superior cerebral in two dogs. In one case in which the normal pressure was very low, about 1·5 of water, it quickly rose to 8 cm., and in the other in which the normal was 6·5 cm. water, after the usual preliminary fall, it rose again to 7·5 cm. The asphyxial gasps when strong may cause a variation in pressure amounting to 1 cm. water.

FIG. 11.



(*c.*) *Venous Pressure Varied by Artificial Respiration.*—By this means the surface may often be made to recover completely, or nearly so.

Conclusion.

The foregoing experiments show clearly that the elastic recoil of the living brain is due primarily to the elasticity of the brain substance, and is not due to the pressure in the arterial system (general).

The recoil, however, varies notably with changes in the pressure in the venous system (cerebral).

DESCRIPTION OF DIAGRAMS.

The continuous lines represent the curves of the variations in level of the brain surface produced by pressure and otherwise. The dotted lines represent the height of the blood pressure.

The times in which compression and recoil are measured are noted above the diagrams in seconds. The enumeration of seconds always commences afresh at the point at which the weight is removed.

Fig. 3. 50 grams applied for 1 minute. This diagram shows typically the characters of the excursion and recoil.

Fig. 4. 50 grams applied for 1 minute. Between experiments *a* and *b* the brain was allowed to entirely recover its volume, and the animal was then bled to the extent of 150 c.c. This procedure caused a fall of the brain surface to 3·4.

Fig. 5. Shows a typical curve when 50 grams are applied for 4 seconds only.

Fig. 6. The curves as far as * show the concurrent variations of brain surface and blood pressure under the influence of amyl nitrite. At * experiment *a* was performed. Between experiments *a* and *b* the effect of the amyl nitrite was allowed to wear off completely. 20 grams was the weight employed.

Fig. 7. (*a*) was an experiment upon the normal brain.
(*b*) was performed after administration of amyl nitrite. Weight = 50 grams.

Fig. 8. (*a*) performed with a cannula in one superior cerebral vein.
(*b*) performed with the opposite superior cerebral also blocked. Weight = 50 grams.

Fig. 9. (*a*) performed on the normal brain.
(*b*) performed with both external and both internal jugulars clamped. Weight = 50 grams.

Fig. 10. 50 grams applied for 6 minutes. Etherisation diminished at * with a consequent rise of blood pressure.

Fig. 11. 50 grams applied for 30 seconds to a brain which had undergone considerable previous compression. Etherisation diminished at *. Trachea clamped at ⊙.

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[*From the* Proceedings of the Royal Society, Vol. 56.]

"Degenerations consequent on Experimental Lesions of the Cerebellum."

By J. S. Risien Russell, M.D., M.R.C.P., Assistant Physician to the Metropolitan Hospital. Communicated by Professor V. Horsley, F.R.S. Received June 4, 1894.

(From the Pathological Laboratory of University College, London.)

(Abstract.)

The paths which degenerate after ablation of one lateral lobe of the cerebellum, and after extirpation of its middle lobe, are discussed in this paper.

The former operation, viz., removal of one lateral lobe of the cerebellum, results in degeneration of all the peduncles on the side of the lesion, and in the superior peduncle of the opposite side; but no fibres degenerate in the middle or inferior peduncle of the opposite side. The degenerated fibres in the superior peduncle on the side

of the lesion decussate in the posterior quadrigeminal region, and pass to the opposite red nucleus and optic thalamus. None could be traced beyond this point. Those in the opposite superior peduncle represent fibres which degenerate in the cerebellum, passing from the seat of lesion across to the intact half of the organ, and leaving it by this peduncle. These degenerated fibres occupy a special position in the peduncle, a part of it which is comparatively free from degenerated fibres on the side of the lesion, and a part occupied by degenerated fibres on both sides, when the cerebellum is divided into two lateral halves by a mesial incision. These facts are held to controvert Marchi's statement, that none of the peduncles contain commissural fibres.

The degenerated fibres in the middle peduncle, on the side of the lesion, pass chiefly to the grey matter of the opposite side of the pons. Some degenerated fibres from this source pass between the pyramidal bundles, but there is no evidence to support Marchi's observation, that degenerated fibres also pass from this peduncle in the fillet and posterior longitudinal bundle to the corpora quadrigemina and periphery of the antero-lateral region of the spinal cord, and that some pass to the corpus striatum by way of the pyramidal tract.

Of the fibres which degenerate in the inferior peduncle, the majority occupy the lateral region of the medulla, becoming more and more scattered as they pass down. These can no longer be said to form a tract below the level of the superior pyramidal decussation; but a few scattered degenerated fibres occupy the antero-lateral region of the cervical cord, beyond which none can be traced. Degenerated fibres pass to both inferior olives from this peduncle; but no well-marked tract to the opposite inferior olive, as described by Ferrier and Turner, was found. In accordance with these observers, however, no corroboration of Marchi's results was found, in so far as he states that degenerated fibres pass from this peduncle to the ascending root of the fifth, the roots of the cranial nerves through the posterior longitudinal bundles, and the spinal nerves by the descending antero-lateral tract.

In confirmation of Marchi, and contrary to the observations of Ferrier and Turner, degenerated fibres were found in all the peduncles of the cerebellum, after extirpation of its middle lobe. Those in the superior peduncle occupy all parts of it, as seen on transverse section, they decussate in the region of the posterior corpora quadrigemina, and terminate in the opposite red nucleus, beyond which point no degenerated fibres could be traced.

The degenerated fibres in the middle peduncle behave much as do those which result from ablation of one lateral lobe of the cerebellum, and the same may be said with regard to the degenerated fibres in the inferior peduncle. No evidence was found to support Marchi's

statement that degenerated fibres from this source pass to the cranial nerve roots through the posterior longitudinal bundles, and to the antero-lateral columns of the cord by way of the fillet.

With regard to the well-marked antero-lateral tract, which Marchi describes as degenerating throughout the whole length of the spinal cord, it is held, in conjunction with Ferrier and Turner, that no such tract degenerates after lesions limited to the cerebellum. And in support of this negative view being probably the correct one, is adduced the fact that Ferrier and Turner found a similar tract after injury to Deiter's nucleus, as did Mott also, after injury to the posterior column nuclei.

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THE VALUE OF EXPERIMENTAL EVIDENCE IN THE DIAGNOSIS OF DISEASES OF THE CEREBELLUM.

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A REVIEW of the literature in connection with diseases of the cerebellum makes it evident that considerable confusion exists with regard to the symptoms on which we are to depend for the diagnosis of such morbid processes, and for their localisation in one rather than another part of the organ. Much of this confusion appears to be due to the following causes: (1) The discrepancies which exist in the results obtained by different experimental physiologists who have investigated the functions of the cerebellum. (2) A disregard on the part of the clinical observers, of experimental evidence bearing on the question. (3) Faulty attempts to apply experimental evidence in the elucidation of clinical phenomena. (4) A preconceived idea that such and such symptoms cannot be directly due to a lesion of the cerebellum, and that therefore some other explanation for their occurrence must be sought for.

THE ABSENCE OF CHARACTERISTIC SYMPTOMS.

One of the first points which calls for our attention is the fact that extensive disease of the cerebellum may exist in man with next to no clinical evidence pointing to the existence of any morbid condition of this part of the central nervous system. We find it at first difficult to reconcile this with the fact that in animals ablation experiments on the cerebellum result in most profound disturbances of function, even when comparatively small portions of the organ have been removed. And yet nothing is more simple than the explanation of what at first appears to be so irreconcilable a discrepancy. It is perfectly true that the most pronounced disturbances of function result when a part or the whole of the cerebellum is removed; but it must not be forgotten that recovery takes place with marvellous rapidity, each disordered function being in turn compensated for with such exactitude that no one unfamiliar with this would believe that an animal presenting all the disorders of function observable directly after the operation could recover to the extent that it does even in the course of a month. Now, if after removal of a large part of the organ such complete restoration of function can be brought about by compensation through other parts of the central nervous system, what

is more likely than that the slow processes of disease, destroying the substance of the cerebellum only gradually should produce no symptoms as a consequence of the loss of function of the part destroyed, owing to the fact that compensation goes on *pari passu* with destruction, the latter being so slow as to allow the former to keep pace with it, and thus no recognisable evidence of the destructive process in the cerebellum is forthcoming?

We need not look to the experimental side of the question alone for evidence in support of the above proposition, for in morbid processes of the cerebellum occupying precisely the same situation in the organ we meet with the most varying symptoms and all degrees of the same symptom. I am convinced that these various differences depend not so much on the extent of the morbid process as on the rate of its development; the more sudden its onset and rapid its development, the more pronounced are the evidences of disordered function, the more gradual its onset and slow its progress the more likelihood is there to be only slight evidence of disordered function or a complete absence of such. In support of this contention I would adduce the following three considerations: 1. The most sudden of all lesions of the cerebellum in man is a hæmorrhage into some part of its substance, an event which, as we are all aware, is attended by disorders of function of a pronounced character. 2. Abscess of the cerebellum may be of rapid or slow development, and correspondingly we find such cases presenting the most varying evidences of disordered function from pronounced to trivial or completely absent. Of course it is, with some exceptions, almost impossible to fix the exact time that the morbid process has been in existence, so that these cases are only of value in supporting the argument when taken in conjunction with cases of the first and third group. 3. Tumour cases more than any others show how trivial the evidence of disease of the cerebellum may be in conjunction with the most gross changes within that organ. It is no uncommon experience to find extensive new growth in the cerebellum with an almost total absence of symptoms which we are in the habit of associating with tumour in that part of the central nervous system. In this statement I of course exclude such general symptoms as headache, vomiting, and optic neuritis—symptoms common to intracranial tumour in the most varied situations. With this—the most slowly progressing of morbid processes to which the cerebellum is prone—we most commonly meet with an absence of or only trivial indications of disorders of function peculiar to the organ under consideration.

Thus, while with the most sudden of lesions of the cerebellum (hæmorrhage) we meet with the most pronounced symptoms of disordered function, with that of slowest development (tumour), we find least evidence of a similar nature, and with a process which may be rapid or slow (abscess) we meet with variations in symptoms which justify our attributing their variations, in great measure, to the rate at which the morbid process is developed.

There is one other factor which has to be taken into account, more especially in connection with tumours of the cerebellum, and that is, that the morbid process may displace without actually destroying the cerebellar tissue, so that unless the process of extension is rapid the organ is

able to accommodate itself to the altered pressure relations for a considerable time.

Just as all symptoms characteristic of disease of the cerebellum may be absent, so it often happens that we have to depend on one or two symptoms alone for diagnosis. The typical picture, comprising all the various phenomena which may be associated with disease in this part is of exceptional occurrence, so that in any given case we must be prepared to depend on the detection and correct interpretation of one or two phenomena to aid our diagnosis, rather than refrain from diagnosis because the typical picture is not before us. It will, therefore, be instructive to consider separately each symptom in which experimental evidence aids us, and on which we may have to depend largely for the correct localisation of disease in the cerebellum.

Inco-ordination.

Probably no symptom is more closely associated with cerebellar disease than co-ordination. This is not the occasion to discuss the nature and mode of production of this phenomenon; it is sufficient for our present purpose that we recognise that it occurs, and attempt to diagnose the seat of the disease in the cerebellum from a consideration of the characters of the inco-ordination. It may be said at once that experimental, and, in the main, clinical evidence, are at one in ascribing to lesions of the front part of the vermis or middle lobe of the cerebellum instability of such a nature that the tendency is to fall forward, whereas when the posterior part of this lobe is affected, the tendency is for the animal or human subject to fall backward. And yet, that the direction of the fall cannot be relied on absolutely as indicating the precise locality of the morbid process in this lobe in the human subject is made evident by such cases as that recorded by Handford,[1] in which the patient tended to fall backward, and yet the whole of the middle lobe of the cerebellum was destroyed by a sarcoma.

When we turn to consider lesions of the lateral lobes of the cerebellum we find a great want of unanimity of opinion; experimental physiologists and clinical observers are alike at variance as to the direction in which the animal or human subject reels or falls when one or other lateral lobe of the organ is affected. According to one class of observers, in destructive lesions of one lateral lobe the tendency is for the subject to rotate, reel, or fall to the opposite side from the lesion; whereas the other class of observers hold that the instability results in a rotation, reel, or fall to the same side as the lesion. For my own part I have always adopted the former view, and I cannot help thinking that we all mean the same thing, but express ourselves differently. In discussing the subject with Dr. Beevor recently, he made a suggestion which appears to me calculated to clear up a good deal of the confusion which at present exists with regard to this subject. Dr. Beevor's suggestion was that we should describe the direction of rotation as compared to a corkscrew as it is turned in going into the cork of a bottle, or in coming out of one.

Now according to my observations, which lead me to the conclusion that the animal rotates away from the side of the lesion; if the lesion happened to be in the right lateral lobe of the cerebellum the animal would rotate like a screw going

[1] *Brain*, 1892, vol. xv, p. 458.

into a bottle, whereas if of the left lateral lobe, then like a screw coming out of one. To make my meaning clearer, let us suppose that a man with disease of the right lateral lobe of the cerebellum is placed to stand facing the observer, he would tend to rotate in such a manner that his left side would next present itself to the observer, then his back, then his right side, and then his face once more; whereas a man with his left lateral lobe affected, similarly placed, would rotate in such a manner that his right side would first present itself to the observer, then his back, then his left side, and then his face once more.

In making the above remarks with regard to the direction of rotation, it must be clearly understood that I refer to the objective phenomena of reeling or rotation, and not to any subjective sensations experienced by the individual, for in experiments on animals it is of course on the objective phenomena associated with inco-ordination that we have solely to depend. Many of the records of clinical cases are wanting in this respect, inasmuch as it is not definitely stated whether the patient actually fell or tended to fall in a certain direction, or whether there was only a subjective sensation of falling in a given direction. Then again a point which appears to be often lost sight of by clinical observers is the fact that implication of the auditory nerve, by pressure or otherwise, may give rise to inco-ordination. Now in animals[2] irritation or intracranial section of the auditory nerve results in rotation or reeling to the same side as the lesion, so that in the absence of middle-ear disease, deafness, or other auditory phenomena on one side, are of great importance quite apart from the evidence with which they supply us that the lesion of the cerebellum is probably situated on that side, for if neglected by those who consider that in an affection of one lateral lobe of the cerebellum the patient falls to the opposite side, a faulty localisation of the lesion would result if staggering, in reality due to implication of the auditory nerve, were attributed to the cerebellum.

It must further be remembered that, inasmuch as there may be motor paresis of the limbs on one side, the patient may, in such cases, tend to fall to that side in consequence of the inability of the lower extremity to support the weight of the body, and therefore this condition of things must be carefully distinguished from the instability which has already been discussed. The distinction is important, for, as we shall presently see, paresis of one side of the body may result as a direct consequence of a unilateral lesion of the cerebellum, in which case the paresis is on the same side as the cerebellar lesion, and the direction in which the patient would fall in consequence of failure of the lower extremity to support the weight of the body would be to the same side as the lesion, while, as I have already urged, the direction of the fall consequent on loss of balance associated with rotation or reeling, would be to the opposite side, that is, away from the side of the cerebellar lesion.

Motor Paresis.

This leads me to speak of a symptom of cerebellar lesions to which little attention has been paid, and which has not been hitherto recognised as consequent on the cerebellar

[2] *Phil. Trans. Roy. Soc.*, 1894.

defect; I allude to motor paresis involving the same side of the body as the lesion of the cerebellum.

It has, of course, long been recognised that tumour or abscess involving one side of the cerebellum may, by pressure exerted on the pyramidal tract of the same side, occasion paresis of the opposite side of the body in consequence of the pressure being exerted on the pyramidal tract above its decussation. But the cases recorded in which there has been paresis on the same side of the body as that on which the cerebellar lesion has been found *post mortem* have met with no satisfactory explanation. In fact, where an attempt has been made to localise the exact seat of the lesion during life it has resulted in error, inasmuch as a lesion of the opposite side of the cerebellum pressing on the pyramidal tract has been diagnosed, or a lesion of the opposite cerebral hemisphere has been looked for as the probable cause of the motor paresis, which was in reality due to a destructive lesion of the side of the cerebellum corresponding to the paresis.[3]

My own observations on animals[4] leave no doubt in my mind that such paresis on the same side as a lesion of the cerebellum is a direct consequence of the cerebellar defect, and is in no way indirectly induced by pressure on other parts. The precise way in which the cerebellar defect induces this paresis does not so much concern us in a paper of this kind as does the practical question whether motor paresis ever occurs on the same side as a unilateral lesion of the cerebellum. That it does is made evident by the results of my experiments, which are further supported by clinical and pathological facts that have been placed on record, and also by others which have come under my own observation. Among recorded cases of the kind one by Ogle[5] is especially interesting because a cyst the size of a walnut occupied the region of the corpus dentatum on the left side of the cerebellum, and there was loss of power in the left arm and leg during life.[6] When, therefore a patient presents, in conjunction with other symptoms usually associated with disease of the cerebellum, paresis on one side of the body, this symptom properly interpreted becomes a localising sign of the highest significance. It is only when taken in conjunction with other evidences of disease of the cerebellum that we can hope to obtain any useful information from this symptom, however, inasmuch as it may signify a lesion of the same side of the cerebellum, or, if occasioned by pressure on the pyramid, then of the opposite side of the organ. Cases of the latter class are generally accepted, and call for no illustration, but it is otherwise with the former class, of which the following is a good example:

At a recent meeting of the Neurological Society of London, Dr. Acland and Mr. Ballance showed a case of right-sided cerebellar abscess which had been successfully operated on by Mr. Ballance. Before the operation this patient had, in addition to other signs of cerebellar disease, paresis of the right arm and leg, and conjugate turning of the eyes to the left. Now no other lesion of the cerebellum but

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[3] *Cf.* Drummond, *Lancet*, July 28th, 1894.

[4] *Loc. cit.*

[5] *Brit. and Foreign Medico-Chir. Rev.*, 1865, vol. xxxvi, p. 233.

[6] Such loss of power on the same side as a unilateral lesion of the cerebellum has been sometimes erroneously ascribed to pressure on the pyramidal tract below the decussation.

one of the right lateral half of the organ could be responsible for this combination of symptoms, for, had the cerebellar lesion been on the left side, causing the motor paresis on the right side by pressure on the pyramid, the eyes, if deviated, would have been directed to the right and not to the left.

Another instructive case in this connection is one recorded by Vulpian,[7] in which a tuberculous tumour of the right side of the cerebellum was responsible for paresis of the right extremities together with turning of the eyes to the left.

There is one point of difference between animals (more especially dogs) and man, and that is that in the former the hind limb on the side of the lesion appears to be the most paresed, while in the latter, when any details have been given in the record, it is the upper limb which has been noted as chiefly paresed, the lower limb being less so, or apparently escaping in some cases.[8] Instances are not wanting, however, in which the paresis has involved both inferior extremities alone in man, and that even in cases of unilateral lesion of the cerebellum.[9] Similar cases have also been recorded in which a tumour growing from the inferior surface of the middle lobe has exerted pressure on the medulla, and in which the movements of the superior extremities have been perfectly preserved.[10]

Before passing from the subject of motor paresis I must refer briefly to the fact that Dr. Hughlings Jackson has long maintained that in affections of the middle lobe of the cerebellum weakness of the spinal muscles results—an opinion which was also held by Niemeyer.[11] It is not easy to judge of the condition of the spinal muscles in most animals, but I found that monkeys deprived of the whole cerebellum were unable to sit up,[12] a condition probably depending on weakness of the back muscles. A year ago I had the privilege of recording a case, in conjunction with Dr. Hughlings Jackson, in which there was undoubted evidence of weakness of the spinal muscles in a patient the subject of a cyst of the cerebellum which involved its middle lobe chiefly.[13]

Ocular Deviations.

Closely associated with this question of motor paresis of the trunk and limbs is that of the displacement of the eyes, which I believe to be of a paralytic nature also. Formerly the abnormal positions of the globes were attributed to overaction of certain of the eye muscles, that is, they were classed among the so-called irritation phenomena of cerebellar lesions, in which category they have been included even by Luciani[14] in his comparatively recent work on the cerebellum. I have contended that these abnormal positions of the eyes are due, not to overaction of any muscles, but to want of action of certain of them. In other words, that they ought to be classed with the paralytic and not with the irritation phenomena of cerebellar lesions, in support of which contention I have adduced arguments elsewhere.[15]

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[7] *Compt. Rend. Soc. Biol.*, 1861, iii, p. 29.
[8] *Cf.* Macewen, *Pyogenic Infective Diseases of the Brain and Spinal Cord.*
[9] *Cf.* Davidson, *Med. Times and Gaz.*, 1878, ii, p. 218.
[10] *Cf.* Poole, *Lancet*, 1891, ii, 664.
[11] *A Textbook of Practical Medicine*, 1876 (Transl.), ii, 244.
[12] *Loc. cit.*
[13] British Medical Journal, February 24th, 1894.
[14] Il Cervelleto; *Nuov. Stud. d. Fisiol. Norm. e Patol.*, Firenze, 1891.
[15] *Loc. cit.*

Experimental and clinical evidence point to turning of the eyes from the side of the lesion, as the abnormal position which is met with in an uncomplicated unilateral lesion of the cerebellum. Among other cases illustrating this is one of cerebellar abscess, successfully operated on, which has been recently recorded.[16] Luciani[17] found that both eyes turned to the opposite side as a result of ablation of one lateral lobe in animals, while, according to my observations, it is the opposite eye which is chiefly displaced in that direction.[18] In a certain number of cases which have been published convergent strabismus has been noted in which the eye on the opposite side from the lesions has been the more displaced, or in which it was alone displaced.[19] As far as I have been able to ascertain, however, the disease has not been limited to the lateral lobe in such cases, but has extended up to the middle line, or even across to the opposite lateral lobe. But we have another point to consider with regard to these cases and that is generally recognised that, from the length of their intracranial course, the sixth nerves are peculiarly liable to suffer in cases of increased intracranial pressure, so that even where no obvious changes have been detected in these nerves, the pressure may have been sufficient to interrupt the transmission of impressions along them, which would account for the convergent strabismus met with, an explanation especially applicable when both external recti are weak.

It is my belief then that the displacement of the globes, which depend on an uncomplicated defect of one lateral lobe of the cerebellum in man, is that in which both eyes are turned to the opposite side, but instead of the eyes being turned to one side, they may appear to be normal until the patient is asked to look to the side of the lesion, when it is found that such a patient is unable to turn the eyes in that direction, or that the resulting movement is very feeble, and that there is a difficulty in keeping the eyes turned to that side.

Ocular displacements differing from those just described probably indicate defect of the middle lobe if they are directly due to the cerebellar disease, and not secondarily induced by pressure on adjoining parts or extension of the morbid process to these. When there is any evidence of pressure on the auditory nerve it ought to be remembered that this in itself is capable of producing ocular displacement and nystagmus.

Nystagmus.

Nystagmus commonly occurs in association with ocular displacements, the result of weakness of the external muscles of the eyes, or it may occur apart from any such displacement. The experimental evidence points to lateral nystagmus, with the jerks from the opposite side towards the side of the lesion, as being that met with in lesions of one or other lateral lobe, and clinical evidence supports this. My experi-

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[16] Winter and Deanesly, *Lancet*, December 8th, 1894.

[17] *Loc. cit.*

[18] It is necessary for me to call attention to the fact that I observed "skew deviation" only when the animals were under the influence of the anæsthetic, as I have evidently been misunderstood on this point. Reliance must only be placed on the effects observed after the influence of the anæsthetic has passed off when comparing the effects in animals with those resulting from disease in man.

[19] *Cf.* Hadden, *Trans. Path. Soc.*, 1890, xli, 17.

mental results lead me to conclude that any irregular or rotatory nystagmus ought to direct our attention to the middle lobe as the probable seat of the disease, and clinically I have not met with a case in which nystagmus of this nature, depending directly on the cerebellar defect, was present, in which the middle lobe was not involved, whether the lateral lobes were also involved or not. In these statements I, of course, exclude all cases in which the nystagmus is not a direct result of the cerebellar defect, but is secondarily induced by pressure, etc., on other parts—for example, the auditory nerve.

The Attitude.

In animals there is a curious rotation of the neck, so that the side of the face corresponding to the lesion is turned upwards, and at the same time the chin is directed to the affected side. So too the trunk is curved with the concavity to the side of the lesion. Similar twisting of the neck with retraction of the head and curving of the trunk with the concavity on the side of the cerebellar lesion has been met with in man, especially in cases of abscess.[20] These conditions no doubt depend on spasm of the muscles on the side of the lesion, of which we have next to speak in connection with muscular rigidity in the limbs.

Muscular Rigidity.

Muscular rigidity is most marked in the limbs on the side of the lesion,[21] and especially in the fore limb,[22] which is rigidly extended in animals. In the human subject such rigidity has been noted chiefly in cases of hæmorrhage, and also in cases of abscess. When it exists on one side only, it deserves careful consideration in conjunction with the other evidences of unilateral disease of the cerebellum, for it may be either the direct result of the cerebellar defect, or it may be consequent on the morbid condition in the cerebellum exerting pressure on the pyramidal tract above the decussation on one side, and thus causing rigidity in the muscles of the opposite side of the body. So that, like motor paresis, this symptom is only of value in diagnosis when taken in association with others, inasmuch as alone it may indicate disease of either side of the cerebellum according as we interpret it as due directly to the cerebellar defect, or as the result of pressure on the pyramidal tract above the decussation.

Convulsions.

Closely associated with this last symptom is a form of convulsion which has been observed to affect the limbs on the same side as a lesion of the cerebellum.[23] As a rule, the convulsions resemble tetanus seizures rather than those which result from discharges having their origin in the cerebral cortex.

I have not myself made any observations with regard to excitation of the cerebellum in animals; but the results obtained by Ferrier[24] are in accordance with the condition of things occasionally met with in man, for this observer found that movements of a sudden and spasmodic character

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[20] *Cf.* Ballance, *Clinical Journal*, 1893.
[21] *Cf.* Drummond, *loc. cit.*
[22] *Cf.* Macewen, *loc. cit.*
[23] *Cf. Drummond, loc. cit.*
[24] Ferrier, *The Functions of the Brain*, second edition, p. 190.

occurred in the limbs on the same side as the hemisphere of the cerebellum excited. Of course, to both muscular rigidity and convulsion of supposed cerebellar origin it has been objected, and fairly so, that these phenomena may result from pressure on the pons, and where both sides of the body are involved, either in rigidity or convulsion, it must be admitted that there is no satisfactory argument to adduce against this view. The same may be said, and more, when the rigidity or convulsions involve the opposite side of the body to that on which the lesion is situated. Under such circumstances there can be little doubt that these symptoms are consequent on pressure on the side of the pons corresponding to the cerebellar lesion. But it is otherwise when, with a lesion limited to one side of the cerebellum, we meet with rigidity or convulsions involving the muscles of the same side of the body as that on which the cerebellar defect exists. In such cases I am convinced that these phenomena are directly due to the cerebellar defect, and that they are not in any way indirectly induced by pressure on adjacent structures, which could only result in the symptoms being general, or, if unilateral, then limited to the opposite side of the body.

The Tendon Reflexes.

The tendon reflexes present curious differences according as they are observed in animals after experimental destruction of portions of the cerebellum, or in man where morbid processes are responsible for the alterations met with. In animals exaltation of the tendon reflexes is the rule, for, with the exception of the fact that immediately after the operation of removal of the lateral half of the cerebellum the opposite knee-jerk is greatly diminished if not abolished, they are always exaggerated. The knee-jerk on the same side as the lesion is greatly increased in activity immediately after the operation, after which it gradually becomes less so, but even three months after it is still brisker than normal, and the opposite knee-jerk, so much diminished at first, becomes very active also, in fact, almost as much so as its fellow; but at a remote period while it is still more active than normal, that on the side of the lesion can be demonstrated to be a little more active than it is.[25] This last characteristic was well shown in a case of cerebellar abscess, successfully operated on by Mr. Dean,[26] and shown at a recent meeting of the Neurological Society of London. In this case, although the abscess formerly existed on the right side of the cerebellum, both knee-jerks were exceedingly active two years and a-half after the operation, and Mr. Dean was unable to say which was the more so.

While exaggeration of the knee-jerks occurs in cerebellar disease in man, it is quite as common an experience to find them diminished or abolished; and beyond stating that in those cases in which there is evidence of pressure on the pyramidal tract, causing paralysis, the knee-jerk on the paralysed side is exaggerated, it cannot be said that we have any satisfactory clinical data to rely on in attempting to come to a correct conclusion as to what significance exaltation or diminution of the knee-jerks has in conjunction with cerebellar disease. All that can be said is that the experimental evidence points to exaltation of the knee-jerk more marked on one side as

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[25] *Proc. Roy. Soc.*, 1893.
[26] Dean, *Lancet*, July 30th, 1892.

being the result of ablation of the side of the cerebellum on which the knee-jerk is the more active; whereas any marked diminution is to be associated with the opposite side. In either case these statements are only true when the altered condition of the reflexes is directly dependent on some cerebellar defect, and not indirectly induced by pressure on the pyramidal tract.

Anæsthesia.

Anæsthesia is a symptom which, so far as I am aware, has not been met with clinically in any case in which it could be said to be directly due to a lesion of the cerebellum, whereas I have met with it in animals[27] after ablation of one lateral half of the organ, in which cases it has, like the motor paresis, involved the limbs on the same side of the body chiefly, the opposite posterior extremity being only slightly involved, and the anterior escaping altogether. So transitory is this symptom in animals, however, that it is not surprising to me that it is absent in cases of cerebellar disease in man, where, as I have already urged, the processes of compensation go on *pari passu* with the slowly destructive processes of disease.

The only lesions of the cerebellum in which we might reasonably expect to find this symptom present, apart from pressure on sensory tracts, are possibly abscesses of rapid formation, and hæmorrhage producing extensive destruction of the cerebellum. Now in both these classes of cases the probabilities are that the rapid or sudden onset of a lesion at all extensive would be attended with loss of consciousness, so that the patient would be unable to give us the necessary information; and probably by the time that consciousness is recovered the symptom, if even it existed previously, would have disappeared. Nevertheless that such cases are worthy of being carefully tested with regard to the perception of sensory stimuli is evident from what has already been said. Like many of the other evidences of cerebellar disease that have been dealt with in this paper, it is only when carefully considered in conjunction with other symptoms that anæsthesia, if present, can be expected to furnish us with any reasonable guide as to the probable seat of the disease in the cerebellum; or, what is practically the same, help us to decide whether the anæsthesia is a direct result of the cerebellar defect, or whether it is only a secondary result consequent on pressure on sensory tracts.

Concluding Remarks.

Throughout this paper I have attempted, as far as possible, to limit myself to the consideration of those clinical phenomena with regard to which we have experimental data for comparison. In so doing many important clinical aids to the localisation of cerebellar disease have not been discussed, as the space at my disposal would not allow of this. Besides which, the chief object of the paper has been to show how experimental results may aid us in the diagnosis and localisation of cerebellar disease in man, to call attention to certain phenomena not generally recognised as the direct results of defect in the cerebellum, and to offer a different explanation for the occurrence of some symptoms to that which has been formerly accepted.

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[27] *Phil. Trans. Roy. Soc.*, 1894.

DEFECTIVE DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM IN A CAT.

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Introductory Remarks.

I AM induced to place this case of defective development of the central nervous system in a cat on record, because it appears to me to be of more than ordinary interest.

My grateful acknowledgments are due to Professor Victor Horsley for enabling me to carry out the examination of this animal at the Pathological Laboratory of University College. I am also indebted to Professor Boyce for his kindness in bringing to my aid his large experience of the topographical anatomy of the central nervous system of the cat.

It is impossible for me to express too cordially my thanks to Dr. S. W. Carruthers, to whose generosity I am indebted for the valuable animal on which these observations have been made. The symptoms presented by the cat, during life, reminded Dr. Carruthers of some dogs which I had shown at a meeting of the Neurological Society, and on whom I had practised ablation of one lateral lobe of the cerebellum; he therefore showed the cat at a meeting of the same Society, and afterwards gave it to me, to make use of as I thought fit.

On examining the animal, I found that there was evidence of paresis of both posterior extremities and of the

right anterior extremity, which condition corresponded to that met with in dogs after ablation of the right lateral lobe of the cerebellum. It therefore seemed probable that in this cat there must be some lesion, or defect, of the right lateral lobe of the cerebellum. And as will be seen subsequently, the condition found at the autopsy amply confirmed the surmise.

The cat was placed under the influence of chloroform, and killed by an over dose of this anæsthetic. On *post-mortem* examination the skull presented no abnormal features, and, as far as could be ascertained, there was no asymmetry. The membranes were normal, and not unduly adherent to the skull or to the brain. The right cerebral hemisphere appeared to be generally a little smaller than the left, but there was no special defect in any one part of it. The whole brain was below the average size; but there was no evidence of special atrophy or defective development of any part in particular, with the exception of the right hemisphere being a little smaller than the left, as has already been said.

The feature which attracted most attention was the condition of the cerebellum; the whole organ was smaller than normal, and also proportionally, as compared with the cerebrum; but most striking of all was the fact that the right lobe was scarcely a third the size of the left (see fig. 1). The right lobe was diminished in all its dimensions; and the corresponding right half of the pons and medulla shared in its defect, though not to such a marked extent. There was apparently a complete absence of the transverse fibres of the pons on the right side, and the whole of the right side of the pons and medulla were markedly smaller than the left. As far as could be ascertained, this asymmetry was not shared by the spinal cord, the two lateral halves of which appeared to be quite equal.

The cranial nerves were smaller on the right side than on the left; but the spinal ones did not present any detectable difference.

The whole central nervous system was preserved in Müller's fluid for subsequent microscopical examination; the result of which will now be detailed.

Microscopical Examination.

The stain that was chiefly employed in this investigation was Weigert's hæmatoxylin method as modified by Pal, and as further modified by Schäfer. This was variously supplemented by carmine, nigrosin, Delafield's hæmatoxylin, eosine, &c.

After describing the condition of the cerebrum and cerebellum, it will, I think, be best to describe the other defects in the rest of the central nervous system, as they are met with at certain typical levels of the pons and medulla, and then to give a short summary of all the defects which were found in this animal, before discussing the significance of these defects, and the deductions to be drawn from them.

The Cerebellum.

The defective development of the right lateral lobe of this organ, as compared with its left, was even more strikingly brought out on vertical transverse sections being made. The right half of the middle lobe did not appear to share in this defective development of the lateral lobe. Contrary to what might have been expected, the proportion between the different layers of cells of the cortex of this rudimentary right lobe was not altered, and the normal proportion of grey to the immediately subjacent white matter was preserved. The cells of Purkinje were normal in appearance, and in their arrangement, as were the cells of the granular and molecular layers of this rudimentary portion of the cerebellum. Whereas the corpus dentatum was well marked on the left side, its only representatives, on the right side, were a few irregularly scattered cells in the region where it ought to have been, which region was of course also greatly deficient in the amount of white matter. The total quantity of fibres passing to and from the cortex of the right lateral lobe was of course much below the normal, a fact in keeping with the small amount of cerebellar cortex which existed on this side.

The Cerebrum.

Vertical transverse sections through the hemispheres at different points showed less asymmetry than appeared to exist when the brain was viewed as a whole. The grey and white matter were normally arranged, the normal proportion between the two appeared to be preserved, and there was certainly no evidence of gross structural general or local change in either hemisphere. The cortical cells of the left hemisphere showed no evidence of atrophy, and those of the right side were also free from any such defect.

The basal ganglia appeared to be equally and normally developed on the two sides, and there was only a very slight difference in the size of the internal capsule on the two sides, that on the right appearing to be a little smaller than that on he left. But sections through the crura cerebri presented a very different state of things, for there could be no question that the right crus was considerably smaller than the left (see fig. 2). While this striking difference was seen in the size of the crura, the optic tracts appeared to be normally and equally developed on the two sides, and made the asymmetry in the crura the more evident (see fig. 2).

The Region of the Posterior Corpora Quadrigemina.

The asymmetry at this level is exceedingly marked, many of the structures on the right side being almost completely absent. The most striking differences are to be seen in the fillets, superior cerebellar peduncles, pyramids, and corpora quadrigemina; but in addition to these, certain minor differences on the two sides are evident.

The right corpus quadrigeminum is about a third the size of the left (see fig. 3); and the same proportion exists in the sizes of the right and left fourth nerves, as they are seen decussating in the roof of the aqueduct of Sylvius (see fig. 4). While the superior cerebellar peduncle is well marked on the left side, scarcely any trace of this structure can be made out on the right (see fig. 3). The difference in the size of the

descending root of the fifth cranial nerve on the two sides is not so striking, for although that on the right is smaller than that on the left, and its fibres are less regularly arranged (see fig. 3), there is not that pronounced difference which has been noted in connection with other structures already described at this level. Scarcely any trace of fillet fibres exists on the right side, while the left fillet is well developed and stands out prominently (see fig. 3). The pyramid on the right side is extremely diminutive, and contrasts markedly with the well developed left pyramid (see fig. 3).

The Region of Exit of the Sixth and Seventh Cranial Nerves.

Many points call for comment at this level (see fig. 5), and foremost amongst them is the complete absence of the pyramid on the right side, there being no trace of this structure to be seen; while on the left side the pyramid is normal.

The enormous difference in the size of the restiform body on the right side as compared with that on the left is striking, for while the latter is of normal size and appearance, the former is represented by an insignificant bundle of fibres, seen cut transversely and situated just internal to the superficial root of the eighth nerve as it makes its exit. The fibres which represent the right restiform body appear to be normal and are not obviously smaller than those of the left restiform body; but they are more crowded together, there being a marked deficiency in the amount of interstitial tissue. The contrast between the two restiform bodies is better seen at a lower level (as represented in fig. 6), at which level the relative sizes of the ascending root of the fifth nerve and the restiform body, on the two sides, is striking.

To revert to fig. 5, however, in addition to the points already mentioned, we see that the posterior longitudinal bundle is smaller on the right side than on the left. The seventh nerve, seen divided transversely as it lies internally to the sixth nucleus, is distinctly smaller on the right side,

its fibres appear smaller and do not stain as well as do those of the left nerve.

The sixth nucleus on the right side is a little smaller than that on the left, though the cells appear to be about the same size in both. Fewer fibres pass from the right sixth nucleus to the opposite posterior longitudinal bundle, than from the left nucleus.

The sixth nerve is slightly smaller on the right side than on the left; but the difference in size is not nearly so striking as is that between the two seventh nerves, the right seventh being notably smaller than the left. A still greater difference in size exists between the eighth nerves; and the accessory nucleus of the eighth is a trifle smaller on the right side.

Practically no difference in the size of the ascending root of the fifth exists on the two sides (see figs. 5 and 6), but the substantia gelatinosa is a little less on the right side as compared with the left. There is a difference in the size of the two superior olives, that on the right side being considerably smaller than that on the left, though its cells do not appear to be small or shrunken.

There is almost a complete absence of any connections between the right side of the pons and the cerebellum.

The Region of the Inferior Olive.

A section through the medulla at this level presents a curious picture (see fig. 7). The pyramid on the left side is well developed and occupies its normal position, whereas on the right side, where the pyramid ought to be, the inferior olive is situated, with the anterior external arcuate fibres, and in addition, what appear to be a few pyramidal fibres forming its inner and anterior boundary. The inferior olive on the left side is exceedingly poorly developed, and represents about a twelfth part of that on the right side in size.

The lateral medullary tract on the right side is almost completely absent, a distinct concavity existing in the periphery of the medulla in this region, instead of the normal convexity which exists on the left side. The nucleus lateralis

is also almost completely absent on the right side at this level. No trace of Boyce's direct tract,[1] which degenerates downwards after ablation of the cerebral hemisphere on the same side, is to be seen; while on the left side this tract is so prominent as to suggest the possibility of its being hypertrophied.

The ascending root of the fifth is equally well developed on the two sides; and the substantia gelatinosa is almost equal also, though possibly it is slightly less on the right side. There is not much to choose between the funiculus gracilis on the two sides; but with regard to the funiculus cuneatus, there is a marked difference, that on the left being about half the size of that on the right.

In addition to these differences, there is a general deficiency in the formatio reticularis on the right side.

The Region of the Decussation of the Anterior Pyramids.

The first and most important point to be noted at this level is with regard to the anterior pyramids. Whereas that on the left side, in accordance with what we have seen at higher levels, is well developed, there is only the merest trace of a pyramid on the right side, an insignificant bundle of fibres alone representing this structure at this level. But the point of extreme interest and importance lies in the fact that instead of the whole of the fibres in the well developed left pyramid passing across the middle line to the region of the right crossed pyramidal tract, the pyramid bifurcates, and while the majority of its fibres pass to the region of the opposite crossed pyramidal tract, about a fifth of their number pass to the region of the crossed pyramidal tract of the same side, that is, to the left crossed pyramidal tract (see fig. 8). The few fibres occupying the position of the anterior pyramid on the right side are distributed as follows: some decussate and pass to the opposite crossed pyramidal tract, some pass with the bulk of the fibres from the opposite

[1] Boyce, *Proc. Roy. Soc.*, 1894.

anterior pyramid to the region of the crossed pyramidal tract of its own side, while some turn forward into the grey matter of the anterior horn (see fig. 9). The next point worthy of note is the fact that there is a distinct deficiency in the region of the direct cerebellar tract on the right side, owing evidently to absence of this tract. Instead of the contour of the cord being preserved, there is a distinct concavity in the periphery at this region, which contrasts obviously with the normal convexity in the same region on the left side.

The defective development of the funiculus gracilis and funiculus cuneatus, with their nuclei, on the left side, is better seen at this level than in any that have been examined higher up. The funiculus gracilis is a little more than half the size of that on the right side, while its nucleus is only a third the size of that of the other. It is not so easy to judge of the exact amount of diminution in size of the funiculus cuneatus, but its nucleus is a little more than half the size of the nucleus of the right funiculus cuneatus (see fig. 8).

The Spinal Cord.

It is most surprising that, in spite of the complete absence of the right pyramid at certain levels in the pons and medulla, and the evident defective development of the direct cerebellar tract noted at the level of the decussation of the pyramids, there should be next to no asymmetry of the spinal cord. As may be seen even from fig. 10, which represents the upper cervical part of the cord, it is difficult to say that there is any difference on the two sides, and the same holds good in the dorsal region; but in the lumbar there is possibly some evidence of slight deficiency on the left side, chiefly in the region of the left crossed pyramidal tract. Nowhere, throughout the length of the cord, is there that difference on the two sides, which might have been expected, in view of the defects of those systems at higher levels which we know contribute to the formation of the cord.

No minute microscopic differences can be detected in the nerve fibres on the two sides of the cord, and the grey matter

PLATE TO ILLUSTRATE DEFECTIVE DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM IN A CAT.

FIG. 1.

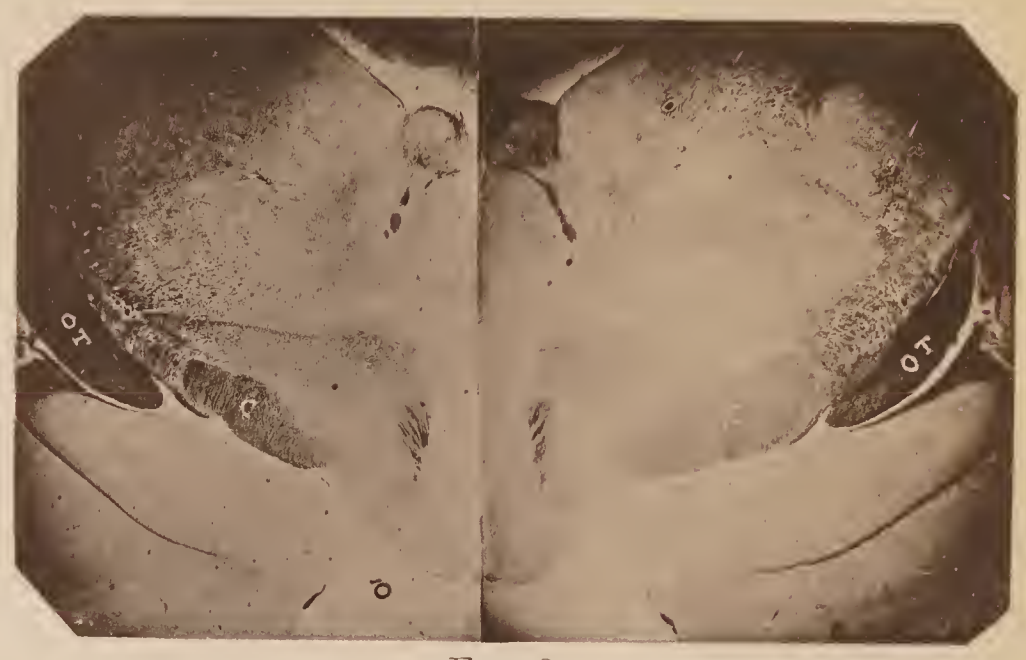

FIG. 2.

FIG. 3.

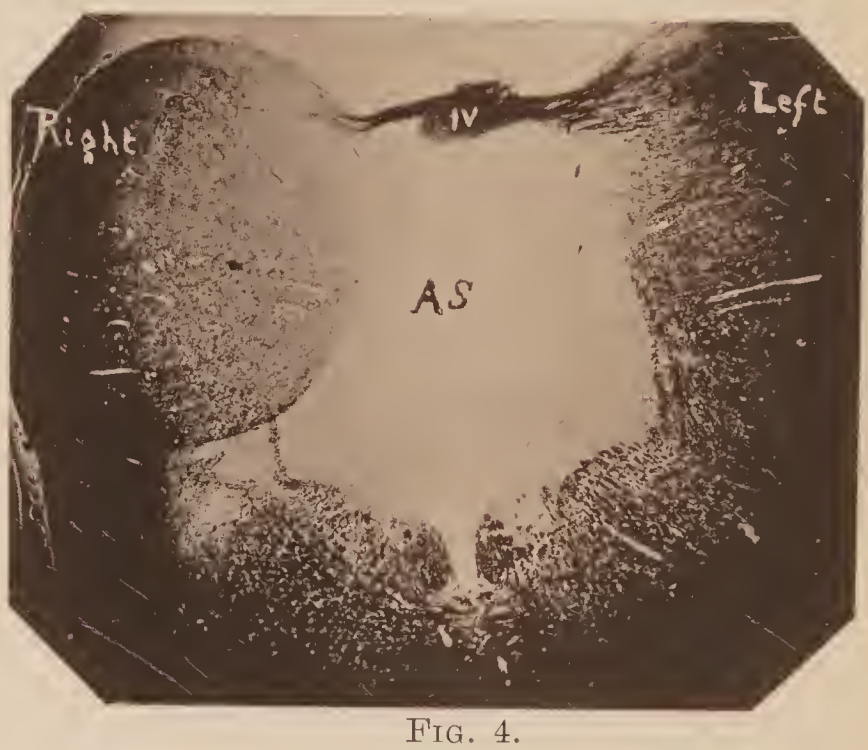

FIG. 4.

FIG. 5.

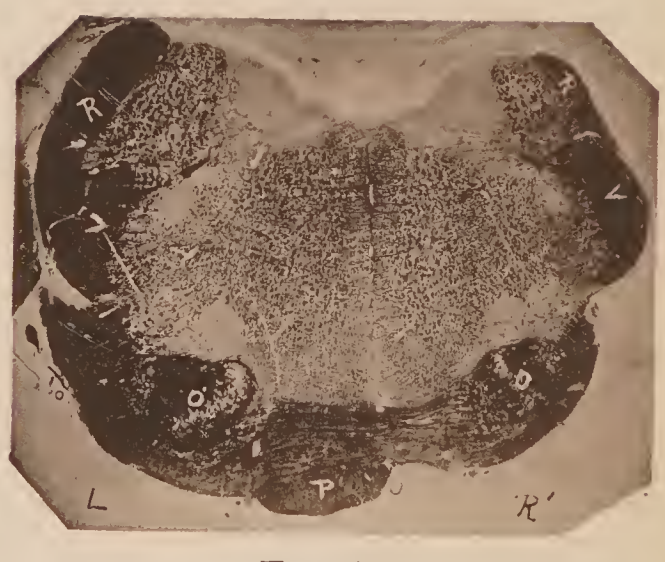

FIG. 6.

PLATE TO ILLUSTRATE DEFECTIVE DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM IN A CAT.

FIG. 7.

FIG. 8.

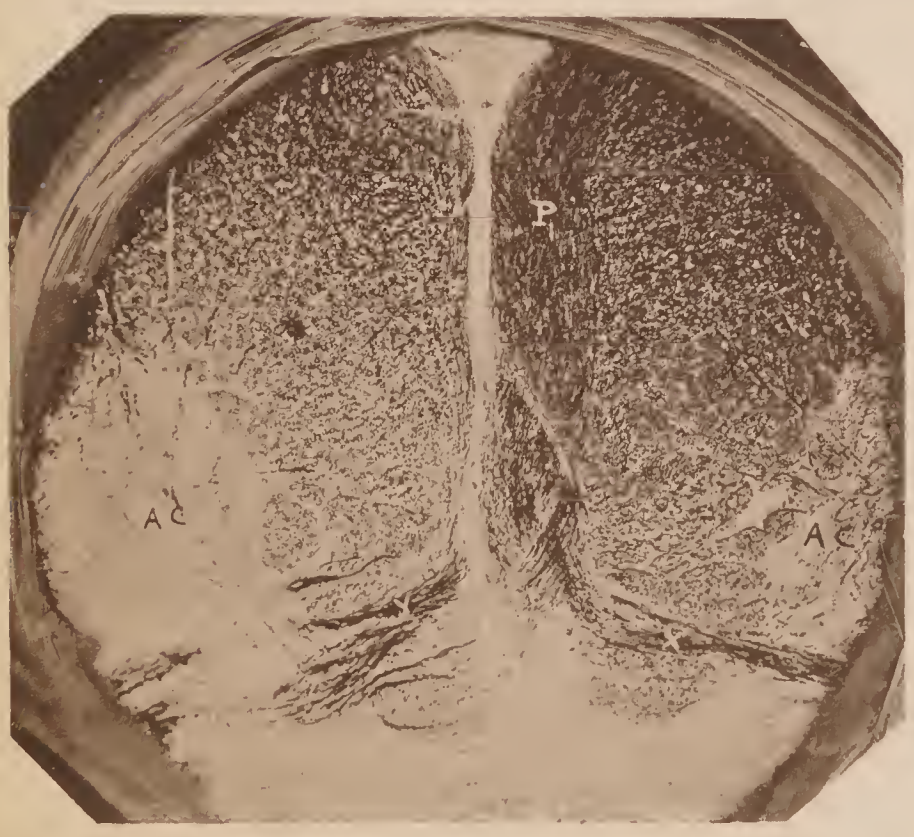

FIG. 9.

FIG. 10.

is normal in amount, as compared with the white, and in arrangement. The minute structure of the grey matter is also normal on both sides, the cells being apparently perfectly natural and showing no structural alterations.

The anterior and posterior nerve roots present no differences on the two sides.

Summary.

It will be profitable for us to review briefly the salient abnormal features presented by this animal, before attempting to discuss the possible significance of certain of these.

First we have the fact that the cerebellum is smaller than normal, as a whole; and that its right lateral lobe is very much smaller than its left.

As to the cerebrum we have seen that only slight differences exist on the two sides in which the right is the slightly defective one, that this slight difference is also apparent in the internal capsule, and that when we come to examine the crura cerebri the right is very distinctly smaller than the left.

The pyramids present many features of great interest. The right pyramid is completely absent throughout the medulla, until the lowest part is reached; but at the level of the decussation a few fibres indistinguishable from pyramid fibres are seen occupying the region of the anterior pyramid on the right side. At the decussation, the normal left pyramid bifurcates, and while the greater number of fibres pass across to the opposite crossed pyramidal tract, a considerable number pass to the crossed pyramidal tract of their own side. Compensation is so complete that, with the exception of possibly a slight difference in the lumbar region of the spinal cord, the crossed pyramidal tract does not appear to be smaller on the left side than on the right.

Practically no trace of fillet fibres can be found on the right side.

All the peduncles of the cerebellum are very deficient, there is practically complete absence of the superior and

middle cerebellar peduncles on the right side, and the restiform body, or inferior cerebellar peduncle, is exceedingly diminutive on the same side.

The cranial nerves are all smaller on the right side than on the left, though they are not all equally so.

The superior olive is slightly smaller on the right side; but the inferior olive is exceedingly well developed on this side, while that on the left side is extremely poorly developed.

The nucleus of the funiculus gracilis and that of the funiculus cuneatus are smaller on the left side than on the right.

It is thus clear that in a pretty universal defect of development of the right side of the pons and medulla there are certain notable structures which do not share to any extent in this defect; they are the ascending root of the fifth nerve, the substantia gelatinosa, the inferior olive, and the nuclei of the posterior columns. Of these structures, two are not defective on the left side either, viz.: the ascending root of the fifth and the substantia gelatinosa; while the inferior olive is markedly defective on the left side, as are the nuclei of the posterior columns, though to a much smaller extent.

Deductions.

That the diminutive right lateral lobe of the cerebellum is a primary condition the result of defective development, and not one due to atrophy secondary to any other lesion of the central nervous system, is evident from the fact that the portion of cerebellar tissue present is normal in structure, neither the cells nor fibres composing it showing any sign of atrophy or other abnormality. It is as if a small portion of normal cerebellar tissue had been left, and the whole of the remainder of the lobe had been cut away. In this respect this case contrasts markedly with two cases of atrophy of the cerebellum in cats recorded by Herringham and Andrewes.[1] The condition of the cerebellum in their cases was apparently primary also, but instead of the cerebellar tissue present

[1] Herringham & Andrewes, *St. Bartholomew's Hospital Reports*, vol. xxiv.

being of normal structure, there was great atrophy of the granular and molecular layers of the cerebellar cortex. Their cases also differed from mine in that the whole cerebellum participated in the atrophy, and not one lateral lobe more than the rest of the organ.

The defective condition of the cerebellar peduncles on the right side calls for no comment, for that the superior peduncle, the transverse fibres of the pons or middle peduncle, and the restiform body or inferior peduncle should be thus defective is only in keeping with the diminutive size of the right lateral lobe of the cerebellum itself.

With so little cerebellar tissue representing the right lateral lobe, it is quite in accordance with our knowledge of the relationship between one lateral lobe of the cerebellum and the opposite inferior olive that the latter should be so defectively developed. The relationship is one which has been well established by pathological observations, and which has been put beyond question by the results of experiment, for it has been found that after ablation of one lateral lobe of the cerebellum the opposite inferior olive atrophies. In the present case it would appear to be not so much a secondary atrophy of the left inferior olive as a defective development of it in association with the defective development of the right lateral lobe of the cerebellum. The fact that the whole of the left side of the pons and medulla is perfectly normal, with the exception of the inferior olive and posterior column nuclei is a most significant one, and points unquestionably to their defectiveness being related in some way to defect of certain structures on the right side. We shall see presently what the probable significance of the defect of the posterior column nuclei on the left side is, and as to the defect of the inferior olive there can, I think, be no reasonable doubt that it is associated with the defective development of the right lateral lobe of the cerebellum. Similarly the well developed inferior olive on the right side, which is otherwise full of abnormalities, is no doubt consequent on the left lateral lobe of the cerebellum being fairly well developed, when compared to the right; a remark

especially applicable to the state of development of the corpus dentatum on the two sides.

This case points to the crossed relationship between one lateral lobe of the cerebellum and the opposite cerebral hemisphere as not being one in which the opposite cerebral hemisphere atrophies, or is defectively developed, in consequence of the abnormality of the lateral lobe of the cerebellum. Congenital cases of atrophy of one lateral lobe of the cerebellum and of the opposite cerebral hemisphere are always open to question as to which is the primary condition and which is the secondary. In thirteen cases, collected by him, Turner[1] concluded that the cerebellar atrophy was secondary to the cerebral. That one lateral lobe of the cerebellum may atrophy in consequence of damage to the opposite cerebral hemisphere is strikingly proved by a case published by Ferrier,[2] in which the one cerebral hemisphere had been converted practically into a cyst, by a hæmorrhage, and in which there was well-marked secondary atrophy of the opposite lateral lobe of the cerebellum. But I know of no similar proof that one cerebral hemisphere ever atrophies in consequence of destruction of the opposite lateral lobe of the cerebellum. A few cases, however, have been recorded in which with well-marked atrophy of one lateral lobe of the cerebellum there has been slight atrophy of the opposite cerebral hemisphere,[3] and Wagner[4] states that he found atrophy of the cerebrum after removal of the cerebellum in pigeons; but this result stands alone, and is open to question. No other observer has recorded atrophy of the cerebrum consequent on ablation of the cerebellum, so far as I am aware; and my own results of extirpation of parts of the cerebellum in dogs forbids my concluding that one hemisphere of the cerebrum atrophies in consequence of destruction of the opposite lateral lobe of the cerebellum. That the one half of the cerebellum exercises a very marked

[1] Turner, *Schmidt's Jahrb.*, 1856, vol. xc., p. 32.
[2] Ferrier, BRAIN April, 1882.
[3] *Cf.* Weber, Cramer, &c.
[4] Wagner, *Journ. de Physiol.*, 1861, vol. iv., p. 394.

influence on the opposite half of the cerebrum has been strikingly demonstrated by certain of my experiments,[1] which leave little doubt that one lateral half of the cerebellum exercises a control on the cortical cells of the opposite cerebral hemisphere.

In the case we are at present considering, although there is very great deficiency of the right lateral lobe of the cerebellum, there is no sign of atrophy or other defect of the left cerebral hemisphere. On the contrary, it is the right cerebral hemisphere which is slightly smaller than its fellow, a condition which is probably part of the general defect on the right side of the central nervous system, and consequent on some common cause, with these other defects, and not in any way specially associated with, or secondary to, the defective development of the right lateral lobe of the cerebellum.

As we are considering the question of crossed relationships, it will be as well for us to inquire into the probable significance of the fact that the posterior column nuclei are smaller on the left side, which, with the exception of the inferior olive, is otherwise quite normal. That these nuclei should be smaller on the left side is only what we are led to expect from the complete absence of the fillet on the right side, for the relations of the fillet to the opposite posterior column nuclei is well recognised. Indeed, it is a matter for surprise that with apparently so complete an absence of fillet fibres on the right side the nuclei of the funiculus gracilis and funiculus cuneatus should not have been considerably smaller than they are; especially when we remember that nothing abnormal could be detected in the basal ganglia.

It only remains for us to consider the defects met with in the pyramidal system, and their probable significance. The internal capsule being a little smaller on the right side than on the left is of course in keeping with the fact that the right hemisphere generally is a little smaller than the left. The size of the right crus cerebri is also in keeping with this;

[1] *Phil. Trans. Roy. Soc.*, 1894.

but neither the size of the capsule nor of the crus prepares us for the complete absence of the right pyramid at a lower level. With such a complete absence of the pyramid on the right side, one would have been justified in looking for a greater diminution in the size of the crus and internal capsule, and certainly also in the cortex of the right cerebral hemisphere.

It is customary to designate those fibres which occupy the ventral aspect of the mesencephalon, in the region of the posterior corpora quadrigemina, pyramidal fibres ; but that this is probably not strictly correct is rendered likely from the condition met with in this animal. We have seen that in the region of the corpora quadrigemina there is a distinct bundle of fibres occupying the region of what is generally looked on as pyramid, on the right side, though the bundle is very much smaller than the corresponding one on the left side. It is difficult to see how, if this bundle of fibres on the right side is wholly made up of pyramidal fibres, there should not be a trace of them to be found in the region of the pyramid at a slightly lower level. Boyce[1] has shown that pyramidal fibres leave the pyramids at all levels in their course, but the number of fibres which thus leave the pyramids under normal conditions are not sufficient to account for the entire disappearance of so considerable a bundle in so short a vertical space. It seems to me far more reasonable to suppose that the fibres forming the bundle in question in the posterior quadrigeminal region are not pyramidal fibres at all, but are of a totally different nature. If this be so, then it appears to me that it would be far more correct to call the bundle at present called pyramid, in the region of the posterior corpora quadrigemina, crural fibres, for as in the crus, so here, there are other fibres in addition to the pyramidal ones. I am thus inclined to believe that under normal circumstances there are certain other fibres contained in the bundle in question together with the pyramidal fibres, and that in this animal these fibres alone exist, while there are no pyramidal fibres contained in the bundle.

[1] Boyce, *Proc. Roy. Soc.*, 1894.

At the level where the anterior pyramids decussate there are two points which call for our consideration. In the first place we have seen that although the pyramid is completely absent on the right side at certain higher levels we have in this region certain fibres occupying the position of pyramidal fibres, indistinguishable from such fibres, and behaving like pyramidal fibres in many respects, for while some go to the anterior horns, others pass to the crossed pyramidal tract of the same side, and some to this tract on the opposite side. It is useless to speculate on the possible source from which these fibres are derived, but their presence points to the probability that just as fibres leave the pyramidal system at different levels, so fibres are added to it at certain levels. I see no other way of explaining the existence of these fibres. If this be the true explanation of their presence, it is clear that the generally accepted belief that all the pyramidal fibres are derived from the cerebral cortex, would require modification. The other point of interest with regard to the pyramidal fibres at the decussation is the fact that while the bulk of the fibres contained in the left or normal pyramid cross to the opposite crossed pyramidal tract, a considerable number pass to the crossed pyramidal tract of its own side. This state of affairs entirely conforms with the results obtained by Mellus[1] and Sherrington[2] who on extirpation of limited foci of the cortex of one cerebral hemisphere of monkeys found that at the decussation of the anterior pyramids the majority of the degenerated fibres passed across to the region of the opposite crossed pyramidal tract, but that a few degenerated fibres passed to the crossed pyramidal tract of the same side as the hemisphere from which the portion of cortex was removed. In my animal the proportion of fibres passing to the crossed pyramidal tract on the same side, that is, on the side of the normal pyramid, were considerably in excess of the proportion met with by Mellus[3] in monkeys. Possibly this is an attempt to com-

[1] Mellus, *Proc. Roy. Soc.*, 1894.
[2] Sherrington, *Lancet*, 1894.
[3] *Loc. cit.*

pensate for the absence of the pyramid on the right side at a higher level and the consequent meagre supply of pyramidal fibres to the left crossed pyramidal tract. This effort at compensation on the part of the normal pyramid accounts in great measure, no doubt, for the comparative symmetry of the spinal cord in the region of the crossed pyramidal tract; but whether it wholly accounts for it may be open to question.

DESCRIPTION OF FIGURES.

FIG. 1.—Represents the cerebrum and cerebellum of a cat, and is intended to show that the whole cerebellum is smaller than normal but that the right lateral lobe is much smaller than the left.

R. = Right. L. = Left.

FIG. 2.—Is from a transverse section in the mesencephalon, and demonstrates that while the optic tracts are comparatively equal in size the right crus cerebri is considerably smaller than the left.

C = Crura cerebri. O. T. = Optic tracts.

FIG. 3.—Indicates the appearances met with on transverse section through the region of the posterior corpora quadrigemina. The right corpus quadrigeminum is obviously much smaller than the left, and there are far fewer crural fibres on the right side, on which side there is almost a complete absence of the fillet and superior cerebellar peduncle.

C. = Crural fibres.
F. = Left fillet.
S. = Left superior cerebellar peduncle.
D. V. = Descending root of fifth nerve.
R. = Right. L. = Left.

FIG. 4.—A section through the decussation of the fourth nerves in the roof of the aqueduct of Sylvius, and shows that the right nerve is much smaller than the left.

A. S. = Aqueduct of Sylvius. IV. = Fourth nerves.

FIG. 5.—Represents a transverse section through the lower part of the pons; the most marked feature at which level is the entire absence of the pyramid on the right side.

P. = Left pyramid.
A. V. = Ascending root of fifth nerve.
O. = Superior olive.
VI. = Sixth nerve.
VII. = Seventh nerves, longitudinally and transversely divided.
R. = Right. L. = Left.

FIG. 6.—Is from a transverse section a little below the level from which fig. 5 was taken, and in addition to the absence of the right pyramid, it is intended to show the insignificance of the right restiform body as compared with the left.

R. = Restiform bodies.
V. = Ascending root of fifth nerves.
O. = Superior olives.
P. = Left pyramid.
R′ = Right. L. = Left.

FIG. 7.—Is a section of the medulla oblongata, made transversely through the level of the inferior olive, which is well marked on the right side and extremely diminutive on the left side. The pyramid and lateral medullary tract are absent on the right side.

G. = Funiculus gracilis.
C. = Funiculus cuneatus.
S. G. = Substantia gelatinosa.
L. M. T. = Lateral medullary tract.
P. = Pyramid.
O. = Inferior olive.

FIG. 8.—Is from a transverse section through the decussation of the pyramids, and shows that while the bulk of fibres from the intact pyramid pass to the opposite crossed pyramidal tract, some pass to the crossed pyramidal tract of the same side.

P. = Left pyramid.
X. = Fibres going from the left pyramid to the crossed pyramidal tract on the same side.
G. = Funiculus gracilis.
C. = Funiculus cuneatus.

FIG. 9.—Is from the same level as the last, but more highly magnified.

P. = Left pyramid.
A. C. = Anterior horn.
X. = Fibres from pyramid to left crossed pyramidal tract.
T. = Fibres from pyramid to right crossed pyramidal tract.
Z. = Fibres in position of right pyramid.

FIG. 10.—Represents a transverse section through the upper part of the cervical cord and shows that the two lateral halves of the cord are as nearly as possible equal.

[*From the* Proceedings of the Royal Society, Vol. 57.]

"On the Changes in Movement and Sensation produced by Hemisection of the Spinal Cord in the Cat."

By Charles Devereux Marshall, F.R.C.S. Communicated by Professor V. Horsley, F.R.S. Received January 31, 1895.

(Abstract).

The present research was undertaken in order to determine more exactly the nature and origin of epileptiform convulsions and the paths in the spinal cord by which both afferent and efferent impulses are transmitted.

The method employed was as follows :—

Hemisection of the spinal cord was performed in the lower dorsal region on the right side, the animals being anæsthetized with ether and strict antiseptic precautions being observed.

The animals were kept alive for different periods of time after the operation, and the effects produced on the voluntary movements, sensibility, and the reflexes were carefully noted.

After death the spinal cords were at once removed, and after hardening and staining, by Marchi's method, both the lesion and the tracts of degeneration were investigated by microscopic examination. There were 16 experiments performed.

The following results are briefly what were obtained.

(*a.*) *Motion.*—After hemisection of the cord there is immediate paralysis of the limb below, and on the same side as the section, this remains for a time, and then gradual recovery takes place to a greater or less extent; sometimes the recovery is so complete that it is with difficulty that one can determine which was the paralyzed limb. At other times more or less permanent weakness is left so as to cause a limp when walking, foot-drop is not infrequently seen and the animal does not appear to appreciate correctly the position that the leg occupies.

(*b.*) *The Reflexes* are, as a rule, greatly exaggerated below and on the same side as the lesion, and sometimes continue so for a long period; in many cases they get less as time goes on; occasionally they are not so well marked as on the opposite or uninjured side.

(*c.*) *Sensation.*—This is always interfered with on the side of the lesion. Painful sensations, such as those produced by the prick of a pin, or by touching the foot with a piece of wire which is slightly heated, appear to be felt on both sides, and this was well seen in the monkeys which were used as control experiments; but the evidence seems to show that these painful sensations are more quickly felt on the non-paralyzed than on the paralyzed side, and also that the animal does not localize the painful spot on the injured side with anything like the precision that it does on the unaffected side.

Tactile sensations, such as those produced by the presence of a small clip applied to the skin, are only felt on the non-paralyzed side; the animals were frequently seen to remove the clip from this side, but unless their tails touched it when placed on the paralysed limb, or their attention was directed to its presence in some such way, no notice whatever was taken of it.

The same result was seen with the cold-water test. When water was brought in contact with the feet, the unaffected limb was at once withdrawn and the water licked off it, while on the opposite side the foot was allowed to stand in a pool of water without any notice being taken of it.

Microscopic Examination of the Spinal Cords.

The portions of the cords containing the lesion were carefully examined for the purpose of ascertaining their exact extent, and a full description is given in the paper.

The following is a short description of the degenerations found in the cord.

(1.) *Descending Degenerations.*—These degenerations were confined almost entirely to the side that was cut, and they occupied the direct and crossed pyramidal tracts; a few scattered degenerated fibres were seen in the antero-lateral tracts of both sides; this was especially marked in the cases where a small part of the opposite half of the cord had become accidentally injured.

(2.) *Ascending Degenerations.*—These degenerations were not entirely confined to the side of the lesion.

The tracts that contained most of the degenerated fibres were the column of Goll, the direct cerebellar tract and the antero-lateral tract. Some degenerated fibres were usually found in the opposite column of Goll, and also in the antero-lateral tract of the uninjured side.

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AN EXPERIMENTAL INVESTIGATION OF EYE MOVEMENTS[1].

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(*From the Pathological Laboratory of University College, London.*)

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I. Introductory remarks.

The opportunity now afforded me of expressing my great indebtedness to Dr Hughlings Jackson for the valuable suggestions which have led to the investigation of some of the points dealt with in this paper, is one which I embrace with very great pleasure. My researches in connection with the points suggested by him have yielded results which entirely confirm his surmises.

It is with as much pleasure that I express my sincere thanks to Professor Victor Horsley for allowing me to carry out the investigations in the Pathological Laboratory of University College.

The present research, which was commenced eighteen months ago,

[1] Part of the expenses connected with this investigation have been defrayed by a grant from the Scientific Grants Committee of the British Medical Association.

deals with ocular movements as influenced by cerebral and cerebellar conditions; and dogs have been exclusively used for the investigations, except in connection with those concerned with the cortical representation of ocular movements, which have been conducted on monkeys. It may be as well to say with regard to the latter experiments that they are not intended to represent any attempt at precise localisation of ocular movements in the cerebrum, but simply to establish the fact that movements other than that of conjugate turning of the eyes to the opposite side, are represented in the so-called eye-area of the cerebral cortex.

II. **Previous researches bearing on the subject.**

Ferrier[1] found that excitation of the posterior half or two-thirds of the superior and middle frontal convolutions resulted in movement of the head and eyes to the opposite side, in connection with certain other effects.

Horsley and Schäfer[2] confirmed Ferrier's observation, but obtained the movements of the head and eyes on excitation of a more extended area of the cerebral cortex than that marked 12 in Ferrier's diagrams. It "comprised an oblong portion of the surface of the frontal lobe, extending from the margin of the hemisphere, round which it dips for a short distance, outwards and somewhat backwards to the upper and anterior limit of the face-area. Posteriorly it is bounded by the arm-area, and in front by the non-excitable portion of the lobe. It extends, therefore, in front as far as the extremity of the præcentral sulcus, and it includes the middle part of the frontal lobe above the antero-posterior limb of that sulcus, the part included in the angle formed by the antero-posterior and vertical limbs of the sulcus, and perhaps a small portion of the ascending frontal gyrus close to the vertical limb of the same fissure."

It was reserved for Beevor and Horsley[3] to demonstrate the possibility of separating the area, excitation of which evoked movement of the head from that, excitation of which resulted in turning of the eyes to the opposite side, and of further differentiating the lateral movements of the eyes.

Turning of both eyes horizontally to the opposite side was rarely

[1] Ferrier. *Functions of the Brain*, 2nd Ed. 1886, p. 242.
[2] Horsley and Schäfer. *Phil. Trans. Roy. Soc.* Vol. CLXXIX (1888), B. 20.
[3] Beevor and Horsley. *Ibid.* B. 28.

met with as a primary movement, but was best represented in the convolutions situated in front of the præcentral sulcus, and to a less degree behind the sulcus which Professors Horsley and Schäfer provisionally named "y" (see fig. 1); movement of both eyes to the

Fig. 1. (After Beevor and Horsley.) From a photograph of the external surface of the right half of the brain of a monkey (Macacus sinicus). *Sulci.* *Sy.A.* Fissure of Sylvius, anterior limb. *Sy.P.* Fissure of Sylvius, posterior limb. *R.* Fissure of Rolando. *PO.* Parieto-occipital fissure. *IP.* Intra-parietal sulcus. *Pc.* Præcentral sulcus. *v. w. x. x'. y. z.* Sulci so named. *Convolutions or Gyri.* *F.* Lip of frontal lobe. *IF.* Inferior frontal. *AP.* Ascending parietal. *SF.* Superior frontal. *AF.* Ascending frontal. *O.* Occipital lobe.

opposite side and upwards was very rarely observed, and only in centres 15, 16, 17, 19, 20, and very slightly at 33 and 31. (See fig. 2.) Movement of both eyes to the opposite side and downwards was only noticed twice, and at centre 22 in both instances (see fig. 2). Limited rotation of the eyes through a few degrees, such as would suffice to restore the direct position of the visual axes, if the eyes happened to be in position of slight conjugate deviation towards the hemisphere stimulated was observed frequently when the centres 28, 28*a*, 26*a*, 26*b*, were excited. Nystagmus was occasionally observed in connection with centres 15, 16, 29, consisted in rapid jerking movements towards the opposite side, and was ascribed to fatigue.

Sherrington[1] experimenting on monkeys, found that when the third and fourth cranial nerves were divided on the left side, excitation of the frontal cortex of the left cerebral hemisphere, by means of the induced current, resulted in conjugate deviation of both eyes to the right, as before the nerves were divided.

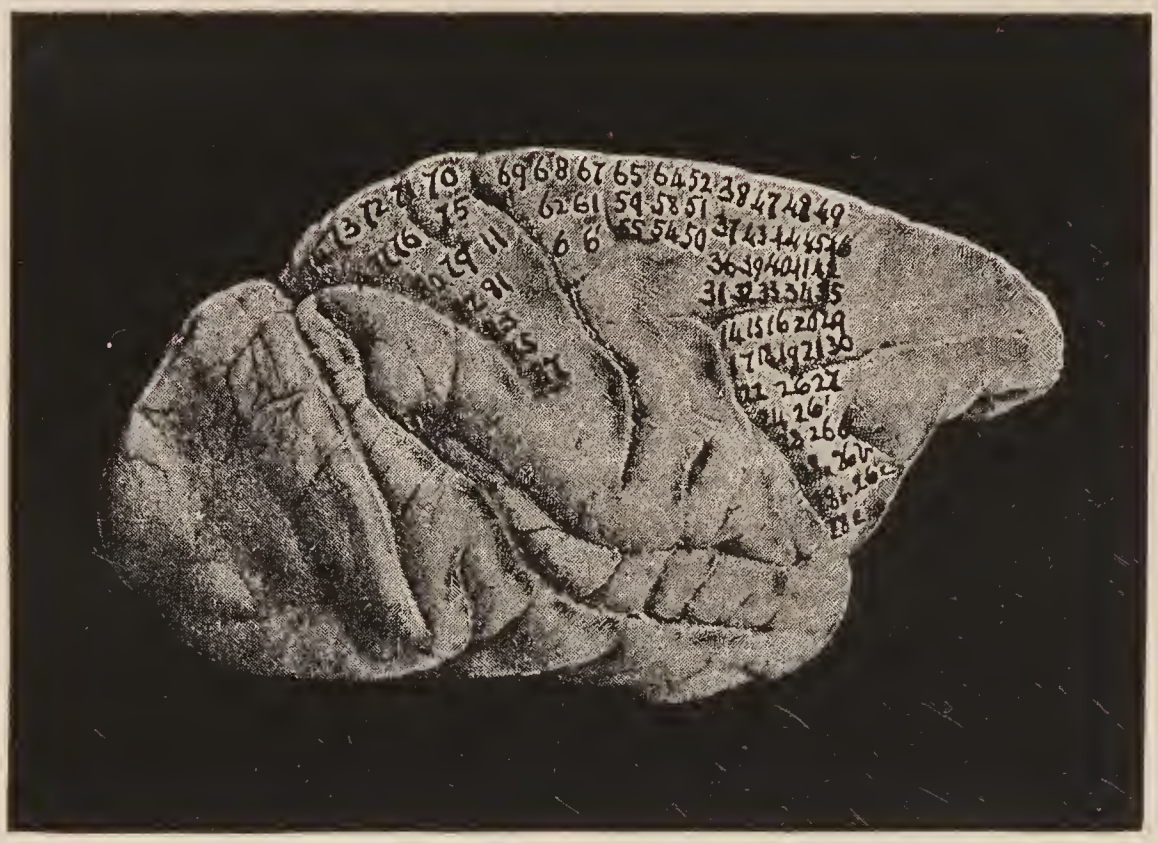

Fig. 2. (After Beevor and Horsley.) From a similar photograph to fig. 1, and shows the area of the cortex, which was the subject of their paper; the numbers denote the different individual points of stimulation, of which 74 are given. Each number denotes a centre of the size of 2 sq. mm.

This movement was obtained even better by exciting the posterior eye-area of Ferrier and Munk. In another series of experiments the sixth cranial nerve was divided on the left side and the frontal cortex of the right hemisphere stimulated, when the right eye moved to the left sharply, while the left eye either did not move, or merely shifted sluggishly up to the full primary position, but not beyond it. These and other similar experiments lead this observer to conclude that the activity of the straight muscles of the eyeballs can be directly inhibited by appropriate excitation of certain parts of the frontal cortex, and still better, of the occipital region, of the hemisphere of the side opposite to the muscle.

Such are the experimental researches which have dealt with the influence of the cerebral cortex on ocular movements in the monkey. I

[1] Sherrington. *Proc. Roy. Soc.* 1893, Vol. LIII. p. 407.

will now briefly allude to those investigations into the functions of the cerebellum which have pointed to any influence of the cerebellum on these movements.

One of the earliest records we have of experiments on the cerebellum is that by Saucerotte[1], who, among other points, concluded that the eyes are innervated from this organ. But the position of the eyes after lesions of the cerebellum or its middle peduncles was more fully described by Magendie[2], who, experimenting on rabbits, found that section of one peduncle resulted in displacement of the eye on the same side downwards and forwards, and that of the opposite side upward and backward. When the peduncle of the opposite side was subsequently divided the eyes returned to their normal positions. An incision into one side of the cerebellum, separating a fourth part of the organ from the remaining three-fourths, was responsible for the same displacement of the globes as after section of the peduncle on the same side. A similar incision subsequently practised on the opposite side was followed by return of the eyes to their normal positions. When the cerebellar lesion was effected on the right side, and the left peduncle was afterwards divided, the eyes instead of returning to their normal positions after the second operation, assumed the position which is met with on section of the left peduncle alone. He also found that when the cerebellum was divided into two lateral halves an extraordinary amount of agitation of the globes resulted.

Gratiolet and Leven[3] appear to have been the next observers who had their attention called to the condition of the eyeballs after experimental lesions of the cerebellum. They found that a vertical incision into the centre of one lateral lobe resulted in displacement of the opposite eyeball forward and upward, while that on the same side was displaced downward and backward.

Leven[4] working in conjunction with Ollivier produced lesions of the cerebellum of guinea-pigs by passing a well-tempered steel needle through their skulls, and noted, among other symptoms, that strabismus resulted.

Renzi[5], experimenting on fishes, thought that the cerebellum

[1] Saucerotte. *Prix de l'Académie royale de Chirurgie*, 1769, Vol. IV.

[2] Magendie. *Journ. de Physiol.*, 1824, Vol. IV. p. 399.

[3] Gratiolet and Leven. *Compt. Rend. de l'Acad. des Sc.*, 1860, Vol. LI. p. 917.

[4] Leven and Ollivier. *Arch. Gén. de Méd.* 1862, S. 2, T. XX. p. 513; 1863, S. 6. T. I. p. 68.

[5] Renzi. *Annal Univ. d. Méd.* 1864, Vol. CLXXXVII. p. 47.

exercised an influence on vision by regulating the co-ordinated voluntary movements of the eyeballs.

Weir-Mitchell[1] found that most deep cerebellar lesions produced squints.

Ferrier[2] obtained the following results when he practised electrical excitation of the cerebellum in dogs. When the pyramid was the region excited on one side both eyes moved to the opposite side; when the declive, they moved downwards and to the same side as the excitation when this was on one side, but when it was in the middle line both eyes moved downwards simply.

Excitation of the postero-superior lobule of one lateral lobe resulted in rotation of both globes upwards and to the side stimulated; while when the floccular region was stimulated the globes rotated on their antero-posterior axes, to the right or left according to the particular part stimulated.

Luciani[3] found that extirpation of one lateral lobe caused both globes to turn towards the opposite side. He noted strabismus and nystagmus after removal of different parts of the organ; and he classes both the ocular deviations and the nystagmus among what he looks on as irritative phenomena, the result of the cerebellar lesion.

III. **Ocular movements represented in the cerebral cortex.**

As is clear from the historical account of the previous experimental investigations in this connection, none but the lateral movements of the globes have been obtained on cortical excitation by those who have preceded me in this field of research. This being the case, it occurred to Dr Hughlings Jackson that possibly the reason why none but the lateral movements of the eyes had been obtained on cortical excitation, might be that these movements are so much more powerfully represented in the cortex, than any of the other ocular movements, that they overpower the latter when the eye-area is stimulated. He therefore suggested to me that I should first exclude the possibility of the lateral movements taking place, and then attempt to evoke the other ocular movements by excitation of the eye-area of one cerebral hemisphere[4].

[1] Weir-Mitchell. *Amer. Journ. of Med. Sc.* 1869, p. 320.
[2] Ferrier. *The Functions of the Brain*, 2nd Ed. 1886, p. 193.
[3] Luciani. *Il Cervelleto*, Firenze, 1891.
[4] Hughlings Jackson. *Lancet*, April 28th, 1894.

Accordingly, the external rectus muscle of the opposite eye and the internal rectus of the eye on the same side as the hemisphere stimulated, were divided before the induced current was applied to the eye-area of the cerebral cortex, which procedure resulted in the demonstration of the existence of the upward and downward movements of the eyeballs, together with certain other movements of the globes which were also evoked. In addition to dividing both the lateral recti actively concerned in moving the eyeball to the opposite side, the external rectus of the opposite eye was alone divided in one series of experiments, and both lateral recti of the opposite eye in another series. The cerebral hemisphere to be excited was in all cases carefully exposed, great care being taken not to injure the cortex by pressure or otherwise. The dura mater was opened and a flap raised so as to expose the eye-area of the cortex, various points of which were stimulated by means of fine closely approximated platinum electrodes, attached to the secondary coil of a du Bois Reymond's inductorium, supplied by a bichromate cell.

The ocular movements evoked on cortical excitation under the various circumstances that have been detailed were:—

1. A direct downward movement of both globes.
2. A similar upward movement of both globes.
3. A movement of both globes downward and to the opposite side, from the hemisphere stimulated.
4. A similar movement upward and to the opposite side from that stimulated.
5. A movement of convergence, both globes turning inwards towards the middle line.
6. A direct lateral movement towards the side of the hemisphere stimulated.
7. A movement upwards and to the same side.

1. *Direct downward movement.* This could always be obtained with great definiteness, and the chief focus, excitation of which resulted in this movement, was just above the horizontal fissure of the præcentral sulcus (see fig. 3.) The movement consisted in a simple direct downward rotation of the globes without any evidence of convergence or divergence, as far as could be observed.

2. *Direct upward movement.* This could also always be obtained with great precision, and the chief focus, excitation of which was followed by this movement, appeared to be slightly above and in front of the preceding area (see fig. 3). Here again the movement was a

simple one, and did not contain any element of convergence or divergence, as far as could be ascertained.

3. *Rotation downward and to the opposite side.* This combined movement was evoked on excitation of an area the chief focus of which is situated just in front of the vertical part of the præcentral sulcus, just below the level of the posterior end of the horizontal sulcus temporarily called "w" by Beevor and Horsley (see fig. 3). In this case the eyeball did not move either directly downwards or in a

Fig. 3. The external surface of the right half of the brain of Macacus sinicus is represented. The numbers denote the chief foci, excitation of which evoked movements of the eyes other than that of conjugate turning to the opposite side from the hemisphere stimulated. 1. Upward movement of both eyes. 2. Downward movement of both eyes. 3. Movement of both eyes upward and to the opposite side. 4. Movement of both eyes downward and to the opposite side. 5. Convergence.

horizontal plane towards the opposite side from the hemisphere stimulated, but assumed an intermediate position which partook of both a downward and a lateral movement of both globes towards the opposite side.

4. *Rotation upward and to the opposite side.* The chief focus, excitation of which was responsible for this combined movement, was just below the horizontal fissure of the præcentral sulcus (see fig. 3). Like the last movement, it was as it were the result of fusion of two simple movements, viz., simple horizontal movement of the globes to the opposite side, and a direct upward movement of them, the position actually assumed by the eyeball being one intermediate between the two.

5. *Convergence.* Unlike the four movements which have been

already described, this one was not constantly met with in all the experiments; but when it was obtained it was quite distinct and left no doubt as to the precise nature of the movement. The focus, excitation of which evoked this movement, was situated in front of that excitation of which resulted in the combined movement of both globes downward and to the opposite side, occupying a position chiefly below and slightly above the hinder part of the horizontal sulcus "w" which has been already referred to (see fig. 3). This movement consisted in a rotation of both eyeballs inwards, i.e., towards the middle line, and with a slight inclination downwards.

The movements of the eyes towards the side of the hemisphere stimulated occurred so exceptionally, and were so indefinite and inconstant even in the animals in which they were observed, that I do not feel justified in doing more than simply stating that I did exceptionally meet with what appeared to be movements of the globes towards the side of the hemisphere stimulated.

IV. **Reappearance of ocular deviations, artificially produced and recovered from, during narcosis.**

This subject had engaged my attention for some time in connection with ocular deviations, the results of cerebellar lesions, which had been recovered from; but Dr Hughlings Jackson suggested that I should pay attention to the subject in connection with displacements of the globes after cerebral lesions[1].

In these experiments an opening was made in the skull in the prefrontal region of one or other side, over that part of the cortex excitation of which evokes conjugate turning of the eyes to the opposite side in dogs. The dura mater over this region was incised, and a flap of it carefully raised, so as to expose the cerebral cortex without producing any injury to it.

The exact area of the cortex excitation of which evokes conjugate turning of the eyes to the opposite side was next determined by means of the induced current applied to the surface of the brain through the medium of fine platinum electrodes. Part of the area thus mapped out was then excised, the cortex and white matter being removed to the depth of about an eighth of an inch.

The external wound was closed, the edges of the skin flaps being united with aseptic horse-hair sutures, an antiseptic dressing was

[1] Hughlings Jackson. *Loc. cit.*

applied, and the animal was allowed to recover from the effects of the anæsthetic. These operations were conducted under strict aseptic precautions, and while perchloride of mercury lotion (1—1000) was used for the external wound, nothing but boiled normal saline solution was employed after the dura mater was incised.

The result of such an operation was to produce conjugate turning of the eyes towards the side of the lesion of the cerebral cortex, which condition was however recovered from in course of time. As soon as it seemed certain that the globes were no longer in an abnormal position, the animal was anæsthetised either by means of the inhalation of ether or of chloroform, and the position of the eyeballs kept under close observation throughout all stages of the narcosis. At first the globes remained in their normal position, but as the stage of so-called surgical anæsthesia was approached, and before the conjunctival reflex was abolished, both globes began to move into the abnormal position which resulted at first after ablation of the cortex, that is they assumed the position of conjugate turning towards the side of the cerebral lesion, in which position they remained until the animal became profoundly under the influence of the anæsthetic agent. When this stage of profound narcosis was reached the globes once more changed their positions. In order to facilitate description, let us suppose that the portion of cortex was excised on the left side, which resulted in conjugate turning of the eyes to the left, which condition had been recovered from, but had been reestablished during the earlier stages of ether or chloroform narcosis, then in the stage of profound narcosis the left eyeball moved from a position of marked deviation outward to one of slight deviation in this direction, and the right eyeball moved from a position of deviation inward to one of slight outward deviation. In other words, the position of the eyes was then that which is characteristic of the stage of deep narcosis in normal dogs, one of a varying degree of divergence[1].

If the anæsthetic was then discontinued and the animal allowed to recover, the eyeballs again assumed the position of conjugate turning to the side of the lesion, which they did before profound narcosis was induced, in which position they remained, to some extent, for a variable time within an hour or two after consciousness was recovered.

[1] Mercier and Warner, *Brit. Med. Journ.* March 10th, 1877, state that in man deep coma from anæsthetics and from other causes is attended by divergence of the eyes, and independent motion of them.

V. **Position of the eyes of normal dogs during narcosis.** (Control.)

The necessity for careful control experiments in connection with the results which have just been detailed was obvious, so that a large number of normal dogs were subjected to the anæsthetic influences of ether and of chloroform, and the positions of their eyeballs noted at various stages of the narcosis induced by one or other of these agents. It soon became evident that some care was necessary in order to discriminate between voluntary movements of the globes and the involuntary movements which occur at certain stages of the narcosis. It was found that if the animal was placed to lie on one side, while the anæsthetic was being administered, it was apt to turn its eyes to the opposite side, in order to look at the person who was administering the anæsthetic. That is, if the animal was placed on its right side, it was apt to turn both eyes to the left. When this movement occurred it always did so, so soon after the administration of the anæsthetic was commenced, that there was little real difficulty of being certain that it was a voluntary movement. The movement in question took place very rarely, and when it did do so, it was always observed long before any sign of loss of consciousness, or rigidity, had supervened. In some animals, as consciousness was being lost, independent movements of the globes were observed[1]; as a rule the one eyeball moved into some position without its fellow participating in that or any other movement, while at other times both globes moved at the same time but in opposite directions, the resulting position being one of divergence of the globes in some cases. These independent movements of the eyes were by no means constant phenomena, and contrasted, in this respect, very markedly, with a deviation of the eyeballs which occurred with great regularity, and great constancy as regards the position assumed by the globes at a later stage of narcosis. This deviation of the globes took place about the time when surgical anæsthesia was about to be established, and consisted in a turning of both globes to one side, to a greater or less extent. In most dogs the eyes turned to the right, but in a few of those observed they turned to the left. Sometimes the deviation was well marked, at other times it was slight, while rarely it was not observed at all. As a rule the eye which moved outward appeared to be turned more than the eye which moved inward, so that

[1] Cf. Mercier and Warner. *Loc. cit.*

the eyes did not always appear to quite maintain their position of parallelism[1]. When profound narcosis was induced, the eye which was turned outward moved from its position of turning to the right (if this was extreme) to a position of slight turning in the same direction; but if it was only slightly turned outward before, it did not materially alter its position, if, indeed, it did so at all. The eye which turned inward always moved from this position to one of slight turning to the left, so that the two globes diverged. This position was maintained up to the time of death; but like all the displacements of the eyeballs which have been alluded to, it varied in degree. In some dogs it was well marked, in others it was only slight, while in others it was difficult to say that there was even the slightest trace of divergence of the globes. Extreme divergence was never met with; and moderate divergence was the rule.

When the dog was allowed to recover consciousness, the eyeballs simply gradually returned to their normal positions. There was no turning of the eyeballs in any one or other direction such as was met with in dogs recovering consciousness when ablation of part of the cortical centres for conjugate turning of the eyes to the opposite side had been previously performed.

VI. **The influence of the cerebellum on ocular movements.**

(*a*) *Ocular deviations.* After ablation of one lateral lobe of the cerebellum "skew deviation" of the eyes is usually observed while the animal is still under the influence of an anæsthetic agent; the eye on the side of the cerebellar lesion is directed upwards and outwards, while the opposite eye is directed downwards and outwards. But when the effects of the anæsthetic have passed off, the globe on the side of the cerebellar lesion does not continue in its abnormal position; the deviation of the opposite globe, on the other hand, persists for several days, as a rule.

When both lateral lobes of the cerebellum were removed, and the middle lobe alone left intact, both eyeballs rotated downwards and to a variable extent outwards, which deviation persisted for some days. Excision of one half of the posterior part of the middle lobe of the cerebellum resulted in the eye of the same side as the lesion being

[1] This is a point on which it is difficult to be certain in dealing with such slight differences.

turned outwards and downwards; while removal of the whole of the posterior part of the middle lobe was followed by downward deviation of both globes, and slight deviation outwards.

The only effect of total ablation of the cerebellum on the position of the eyes was to produce a variable amount of downward rotation of both globes.

All of these ocular deviations, which result from ablation of the whole, or of parts of the cerebellum, are recovered from after a variable time, depending on the nature of the lesion from which they resulted. If after the globes had returned to their normal positions, ether or chloroform narcosis was induced in the animal the deviation of the eyes, previously consequent on the cerebellar ablation, was re-established.

(*b*) *Nystagmus.* Another phenomenon, connected with the eyeballs, which is consequent on ablation of parts of the cerebellum, or of the whole organ, and which deserves consideration, is nystagmus. Two distinct forms of nystagmus are to be distinguished in this connection; a spontaneous nystagmus which goes on in a definite direction, and quite irrespective of voluntary ocular movements, and the nystagmoid jerks which only occur when the globes are moved voluntarily, and which then take place only in the direction in which the globes are turned.

On ablation of one lateral lobe of the cerebellum, nystagmus is more or less constantly met with for a varying time after the operation, sometimes only persisting for a day or two. It is always lateral in direction, and consists in slow jerks towards the side of the cerebellar lesion, which appear to be more marked in the opposite eye, e.g., if the left lateral lobe of the cerebellum be removed the right eye deviates downward and to the right, and the nystagmoid jerks of both globes are from right to left.

After removal of both lateral lobes of the cerebellum, nystagmus was met with which was upward in direction with a tendency for the upper segment of each globe to rotate from within out, at first. This spontaneous nystagmus was replaced by nystagmus which only occurred when the eyes were moved, and then the direction of it was that in which the eyes were turned; and in the course of two or three days there was no longer nystagmus of any description.

Extirpation of one lateral half of the posterior part of the middle lobe occasioned nystagmus of both globes, the direction of the jerks being to the opposite side and slightly upward, so that if the left half of the posterior part of the middle lobe was excised, the left eye was

directed to the left and downward, while the nystagmus consisted in jerking of both globes to the right and slightly upward.

When the whole instead of the half of the posterior part of the middle lobe was removed, the nystagmus was vertical, both globes being jerked in an upward direction, and sometimes it partook of an irregular rotatory character.

After ablation of the whole of the cerebellum no spontaneous nystagmus was observed, but nystagmoid jerks occurred in connection with both globes, in the direction in which they chanced to be voluntarily moved.

It was frequently observed that after nystagmus the result of cerebellar lesions had been recovered from, if the animal was placed under the anæsthetic influence of ether, the nystagmus returned at a certain stage of the anæsthesia. The stage at which this occurred was just as the globes were about to turn to one or other side; and the nystagmus quickly ceased as anæsthesia deepened and the abnormal position of the eyes was established. This was observed even several months after ablation of one lateral lobe of the cerebellum.

VII. **Control experiments on the labyrinth and eighth nerve.**

These control experiments were instituted with a view to excluding the possibility of the effects obtained on removal of parts of the cerebellum, especially the lateral lobes, being wholly or in part due to interference with one or other, or both of these structures.

The procedures adopted were:—

1. Extirpation of the labyrinth on one side.
2. Intracranial section of the eighth nerve on one side.
3. Chemical irritation of the eighth nerve on one side.

As all these procedures were attended with almost identical results, they will be considered together; but before doing so, it is necessary for me to explain that owing to the impossibility of exposing a sufficient length of the eighth nerve, to apply an irritant to it, without lifting up the lateral lobe of the cerebellum, the irritant was placed on the end of the nerve as it entered the labyrinth. Crystals of chloride of sodium were packed around the stump of the nerve, and kept in position by means of a plug of aseptic wool introduced into the labyrinth.

The ocular displacement met with consisted in a rotation of the globe on the side of the lesion downwards. It was difficult to say whether there was in addition displacement of the globe outward, as

described by Bechterew[1], or inward; sometimes the one, sometimes the other appearing to be the position, while at other times it was impossible to detect any but the downward displacement. Like Bechterew, I found that the opposite eye turned inwards, but I have not met with the upward rotation of this globe, which he also describes.

Nystagmus was always well marked[2], differed in character on the two sides, and varied according to the time after the operation that the observation was made. Directly after the operation there was usually upward nystagmus of the globe on the same side of the lesion, with a varying amount of the inward element, while the opposite globe was the subject of lateral nystagmus, the jerks being outward. The exact character of the nystagmus varied even in the same animal; for example, a dog who was the subject of nystagmus of the character just described, immediately after the operation, was observed to have well marked rotatory nystagmus of both globes two or three hours after the operation, the upper segment of the eyeball on the side of the lesion turning inward, while the same segment of the opposite globe rotated outward.

VIII. **The effects of removing one lateral lobe of the cerebellum and part of the eye-area of one cerebral hemisphere.**

In one series of experiments part of the eye-area of one cerebral hemisphere was removed, and after some days one lateral lobe of the cerebellum was extirpated; sometimes the lateral lobe on the same side was that removed, while at other times it was that on the opposite side. A second series of experiments consisted in removing one lateral lobe of the cerebellum in the first instance, and after the lapse of a few days part of the eye-area of the cerebral hemisphere of the same or opposite side was excised. In a third series of experiments one lateral lobe of the cerebellum and part of the eye-area of the same side were removed at the same time.

1. *Ablation of part of the eye-area of one hemisphere, followed by extirpation of the opposite lateral lobe of the cerebellum.*

Having ascertained to which side the eyes turned in the stage of

[1] Bechterew. *Pflüger's Archiv*, 1883, Vol. xxx. p. 312.

[2] C. F. Cyon. *Pflüger's Archiv*, 1874, Vol. viii. p. 306; Högyes, *Ibid.* 1881, Vol. xxvi, p. 558; Bechterew, *loc. cit.*; Sewall, This *Journal*, 1884, Vol. iv. p. 339, &c.

ether narcosis in which ocular deviation is met with in normal dogs, part of the eye-area, on which that movement is supposed to depend, was excised. The result of this operation was to cause the eyes to turn in the opposite direction, i.e. towards the side of the lesion. As soon as the globes had returned to their normal position when at rest, the opposite lateral lobe of the cerebellum was extirpated. The result of this second operation was to produce a deviation of the eye on the side of the cerebral lesion outwards and to a varying degree downwards, while as far as could be seen there was no appreciable effect on the eye on the side of the cerebellar lesion, i.e. it remained approximately in its normal position after all influence of the anæsthetic had passed off. To make this point clearer, let us suppose that before any operation had been performed the dog's eyes turned to the left, at the particular stage of ether narcosis. Part of the eye-area of the right cerebral hemisphere was removed, which resulted in turning of both eyes to the right. In a few days, when the eyes had returned to their normal positions, the left lateral lobe of the cerebellum was removed, and while the left eye did not appear to be affected by this second operation, the right eye turned to the right with a more or less downward inclination.

In other words the effect produced by removal of one lateral lobe of the cerebellum in an animal deprived of part of the eye-area of its opposite cerebral hemisphere was practically the same as the effect produced in an animal whose eye-areas in the cerebrum were intact. The only point with regard to which I have any doubt is as to whether the amount of downward rotation of the opposite eyeball is as pronounced as when the operation of removing one lateral lobe of the cerebellum is practised in otherwise intact dogs; but as this factor is a variable one even in such dogs, it is of course impossible to be quite certain on this point.

2. *Ablation of part of the eye-area of one cerebral hemisphere, and subsequent extirpation of the lateral lobe of the cerebellum on the same side.*

The same preliminaries were gone through as in the former experiments, and when the eyes had returned to their normal positions, some days after ablation of part of the eye-area of one cerebral hemisphere, the lateral lobe of the cerebellum on the same side was removed. The effect of this second operation was apparently nil as far as the eye on the same side was concerned, and whereas the opposite eyeball turned outward, it did so only to a slight extent, and certainly not to the

extent which one is accustomed to meet with in dogs whose cerebral eye-areas are intact.

For example, suppose the dog's eyes turned to the left at the stage of ether narcosis that has already been described, and part of the eye-area of the right cerebral hemisphere was removed, the eyes then turned to the right. After they had returned to their normal positions the right lateral lobe of the cerebellum was excised when the right eye was apparently unaffected, and the left eye, while turning to the left, did so to a much slighter extent than is usually the case when the right lateral lobe of the cerebellum is removed in a dog whose cerebral eye-areas are intact.

3. *Extirpation of one lateral lobe of the cerebellum, and subsequent removal of part of the eye-area of the opposite cerebral hemisphere.*

These experiments yielded results which were in keeping with those in which the eye-area of one cerebral hemisphere was first removed, and the opposite lateral lobe of the cerebellum excised at some subsequent period. If the dog's eyes turned to the left under ether narcosis before any operation had been performed, ablation of the left lateral lobe of the cerebellum did not appear to affect the left eye; while the right deviated outward that is to the right, and downward. After the right eye had returned to its normal position, ablation of part of the eye-area of the right cerebral hemisphere resulted in both eyes turning to the right.

4. *Extirpation of one lateral lobe of the cerebellum and subsequent removal of part of the eye-area of the cerebral hemisphere on the same side.*

Here again the results were in harmony with those obtained when part of the eye-area of one cerebral hemisphere was first excised, and the lateral lobe of the cerebellum on the same side subsequently removed. Excision of the left lateral lobe of the cerebellum in a dog whose eyes formerly turned to the left in ether narcosis, resulted in the right eye turning to the right and downward, while the left eye was apparently unaffected. When the right eye had returned to its normal position, after the lapse of some days, part of the eye-area of the left cerebral hemisphere was removed, when the left eye turned to the left, while the right eye only turned to a very slight extent, if at all, in the same direction. So that while the left eye behaved as in a dog whose cerebellum was intact, the right eye did not do so, for instead of turning to the left to the same extent as did the left globe, it scarcely turned at all in that direction.

5. *Ablation of part of the eye-area of one cerebral hemisphere, and extirpation of the lateral lobe of the cerebellum on the same side, at the same operation.*

The effect of this double operation was to cause no appreciable turning of the opposite eye from its normal position, while that on the same side turned to the same side; a result in keeping with the last experiments detailed. That is, removal of part of the eye-area of the right cerebral hemisphere, together with the right lateral lobe of the cerebellum, did not cause the left eye to move to any appreciable extent from its normal position, while the right eye turned distinctly to the right. Thus the right eye behaved as in an otherwise intact dog whose eye-area had been excised from the right cerebral hemisphere, while the left eye behaved quite otherwise, for it did not accompany its fellow in its turning to the right. The double effect of the cerebral operation which would have caused it to turn to the right, and of the cerebellar operation which would have been to result in its turning to the left, being to leave it practically in its normal position.

IX. **Discussion of the results.**

1. *Ocular movements represented in the cerebral cortex.*

The results obtained in this connection leave no doubt that, as it was only natural to suppose, all the movements of the eyeballs are represented in the cerebral cortex, and not only lateral movement to the opposite side, that is away from the cerebral hemisphere stimulated.

Dr Hughlings Jackson's suggestion, as to the probable explanation why under ordinary circumstances none but the lateral movements of the eyes to the opposite side can be elicited on excitation of the one cerebral hemisphere, appears to be the correct one. The fact that when lateral movement to the opposite side has been excluded, other movements of the eye can be evoked on excitation of an area in the cortex, which when stimulated, with the muscles whose actions bring about movement of the globes to the opposite side intact, invariably results in this movement alone being performed, is strong evidence in favour of the supposition that the lateral movement of the eyes to the opposite side is so powerfully represented in the cortex that it overpowers all other movements of them. The other ocular movements are as truly represented in the cortex as is the lateral movement of the globes to the opposite side; the only difference is a question of degree in their representation, the latter being more powerfully, or more widely represented than any other ocular movement.

2. *Reappearance of ocular deviations, artificially produced and recovered from, during narcosis.*

The results of those experiments in which ablation of part of the centre for conjugate turning of the eyes to the opposite side was performed, are of interest in several respects. In the first place they illustrate how readily compensation takes place after a destructive lesion of a part of the central nervous system, for we have seen that whereas the first effect of such a lesion was the establishment of a position of the eyeballs in which they both turned towards the side of the injured cortex, in a few days this abnormal position of the globes no longer existed. According to the generally accepted views, the original turning of the eyes is the result of unantagonised action of the muscles which normally move the globes in that direction, and which are innervated by the intact hemisphere; but in what way compensation is brought about, when the deviation is recovered from, is open to speculation. The readiest explanation which offers itself is that as only part of the centre for the movement has been removed, the remaining parts take on the work of the parts destroyed, by a process akin to hypertrophy. Another possible explanation is that compensation is brought about through the agency of the opposite cerebral hemisphere, the paresed muscles obtaining an increased supply of energy from it. A third possibility which suggests itself is that the compensation is brought about through the agency of the cerebellum; and a fourth is that the compensation is the direct result of an altered condition of the centres of the opposite cerebral hemisphere, but that instead of its being the result of an increased supply of energy to the paresed muscles from the centres, it is due to a diminished output of energy to the intact muscles which are mainly innervated from this hemisphere.

In the present state of our knowledge on this subject it would be hazardous to venture any definite opinion as to whether any of the possibilities suggested are responsible for the compensation, and if so to which of them it is to be ascribed. But by examining each a little more in detail, we can, I think, come to some conclusion as to which of the explanations suggested appears to be the most likely.

There would be little to urge against the first explanation offered, were it not for the fact that compensation results even after removal of the whole of the cortical area of one hemisphere excitation of which results in movement of the eyes, though the globes take a much longer time to return to their normal position. This fact does not however

wholly exclude the possibility that compensation is brought about by the remaining cells which are concerned with the production of the movement which is temporarily lost, for the representation of the movement may be more extensive than the results of electrical excitation of the cerebral cortex would lead us to suppose. Dr Jackson is of opinion that this movement may be also represented in the so-called arm and leg areas[1].

The second explanation suggested as possibly accounting for the way in which the compensation results, is to my mind one of the least likely. The degree to which movements of the eyes to the same side are represented in a cerebral hemisphere must be exceedingly slight. When detailing the results of electrical excitation of the eye-area of one hemisphere, we saw that great uncertainty existed as to whether there was ever any definite movements of the eyes to the side of the hemisphere stimulated, so rarely was even a suspicion of such movements met with. So that it seems to me improbable that compensation is brought about by the intact hemisphere taking on the action of the damaged one.

The third explanation which points to the cerebellum as the possible source from which the energy is derived for compensation, is not so easily dismissed. It is quite possible that the compensation is brought about through the agency of the opposite lateral lobe of the cerebellum. Ferrier[2] found that electrical excitation of one lateral lobe evoked movement of both eyes to the same side; Luciani[3] found that both eyes turned to the opposite side after ablation of one lateral lobe; and in my own experiments ablation of one lateral lobe resulted in displacement of the opposite eye to the opposite side. All these observations point to one lateral lobe of the cerebellum as exercising a somewhat similar influence on the ocular muscles as that exercised by the opposite cerebral hemisphere. So that when the cerebral influence has been removed it is possible than an additional amount of cerebellar energy is liberated to compensate for the want.

The fourth or last explanation that has been put forward is also one which bears closer investigation. It is not extravagant to suppose that the amount of motor energy liberated by any centre is proportional, within certain limits, to the amount called for; and that just as the amount of power may be voluntarily varied, so in the case of a constant involuntary liberation of energy the amount may be varied, the variation in this case being brought about reflexly. To apply this principle

[1] *loc. cit.* [2] *loc. cit.* [3] *loc. cit.*

to the case in point, we should have to suppose that the amount of energy liberated by the centres for moving the eyes in one direction is called forth reflexly by the amount of tension to be overcome in the muscles which tend to move it in the opposite direction, and vice versa, the two conditions equalising each other under normal conditions. When the amount of tension is diminished in one set of muscles, as a result of destruction of part of the centre which supplies them with motor power, the reflex call on the centres which innervate the opposite muscles is diminished, so that the centres gradually accommodate themselves to a diminished output of energy just sufficient to antagonise the amount put out by the damaged hemisphere, and not the amount which was normally required to bring about a state of equilibrium, and which resulted in apparent overaction, which was in reality the result of under action of the damaged hemisphere.

These experiments are of further interest in that after the eyes had returned to their normal position they could be made to assume the abnormal position which originally resulted from ablation of part of the eye-area of one cerebral hemisphere, by placing the animal under the anæsthetic influence of ether or chloroform. The reappearance of the ocular displacement during narcosis, appears to me to confirm Dr Hughlings Jackson's view that after destruction of part of the cortical representation for eye movements certain nervous arrangements for some ocular movements are lost for ever[1]. It thus appears that after removal of part of the eye-area of one cerebral hemisphere the nervous arrangements for certain movements for turning the eyes to the opposite side are permanently lost, so that when the animal is placed under the influence of an anæsthetic the few remaining nervous arrangements for ocular movements are abolished before the whole of those for ocular movements represented in the intact hemisphere share the same fate, the result being that the eyes are turned from the intact hemisphere towards that part of whose eye-area has been destroyed.

3. *Position of the eyes of normal dogs during narcosis.*

These control experiments make it evident that under normal circumstances the cerebral centres in the two hemispheres do not succumb simultaneously under the narcotising influence of ether or chloroform. It seems highly probable that the reason why the eyes turn to one side at a certain stage of the narcosis is because the ocular

[1] Hughlings Jackson. *Brit. Med. Journ.* July 14th and 21st, 1888.

representation is unequal in the two hemispheres, that in which there are fewer nervous arrangements for turning the eyes to the opposite side giving out first[1]. This fact would at first sight appear to detract from the observations made after ablation of part of an eye-area of a hemisphere, in which ocular displacements that had been recovered from were reproduced under the influence of an anæsthetic. But in reality it does not alter the significance of those observations, for we have seen that the eyes of an animal which turn, we will say to the right, under the influence of an anæsthetic when the cortical centres are intact, turn to the left under the same influence after part of the eye-area of the left cerebral hemisphere has been removed, even when no displacement of the globes can be detected when the animal is not under the influence of an anæsthetic.

Another point worthy of notice in this connection is the fact that when a dog whose cortical eye-centres are intact, is recovering from profound narcosis, the eyes do not turn to one or other side before returning to their normal position, as is the case with dogs who have been deprived of part of the eye-area of one cerebral hemisphere.

This turning of the eyes to one side in normal dogs under the influence of an anæsthetic, lends weight to the explanation which has been offered to account for the ocular displacement produced by ablation of part of one eye-area and recovered from, but reappearing under the influence of an anæsthetic, for the mechanism by which the displacement is brought about is probably similar in the two cases.

The position of slight divergence assumed by the globes in most cases when the animal is profoundly under the influence of the anæsthetic is evidently due to all the centres which exercise any influence on the muscles of the eyes being as it were drowned, so that the globe simply settles in that position without being pulled on by any of the ocular muscles, all of which are completely out of action.

4. *The influence of the cerebellum on ocular movements.*

(*a*) *Ocular deviation.* Strabismus or ocular deviation of any kind, the result of ablation of part of the cerebellum, is usually ascribed to irritation, by the lesion, to the damaged nerve fibres or remaining nerve centres; but I have urged elsewhere[2] that this view is not in keeping with what we find in other parts of the central nervous system. After

[1] Cf. Hughlings Jackson. *Lancet*, April 28th, 1894.

[2] *Proc. Roy. Soc.* 1894, Vol. LV. p. 57.

ablation of part of the eye-area in one cerebral hemisphere, both eyes turn towards the side of the lesion; now no one would think of ascribing this phenomenon either to irritation of the injured nerve fibres or of the remaining nerve cells which are concerned in the production of the movement, for we are well aware that irritation of this kind would produce turning of the globes in exactly the opposite direction. We therefore attribute the phenomenon to the action of the opposite cerebral hemisphere whose influence is no longer sufficiently antagonised, owing to the deficiency which has been produced in the hemisphere toward which the eyes are turned. Why then, if this be true of the cerebrum, should it not be also true for the cerebellum? I see no reason. Strabismus, or ocular deviation of any kind, consequent on ablation of part of the cerebellum appears to me to be as truly a negative condition, as a similar displacement of the globes following ablation of part of the cerebrum. What part of the central nervous system is more prone to discharge, when irritated, than is the cortex cerebri? Why then should operations be capable of being performed on the cerebral cortex without producing so called irritative effects, while operations in every way similarly conducted on the cerebellum, should give rise to such marked irritation phenomena?

I am supported in my view that strabismus, or any form of ocular deviation, after ablation of part of the cerebellum is a paralytic rather than an irritative phenomenon by the fact that direct excitation of the intact organ, either mechanically or electrically, evokes movement in exactly the opposite direction to that to which the globes turn when ablation of the same area of the cerebellum is performed. A comparison of Ferrier's[1] results, on electrical excitation of the lateral lobe of the cerebellum in the dog, with Luciani's[2] and my own, after ablation of this part of the organ in the same animal, illustrates this point well. Like all other paretic symptoms which result from destruction of parts of the cerebellum, it is open to question whether the effect is due to the taking off of some direct[3] influence of the cerebellum from the muscles, or whether it is due to an indirect effect on the muscles brought about through the agency of the cerebral hemisphere of the same, or opposite side, by the removal of some cerebellar influence from the cells of the cerebral cortex. That the cerebellum exercises an important action on the cerebral cortex, I have shown elsewhere[4]; the results of my

[1] *loc. cit.*

[2] *loc. cit.*

[3] By "direct" I mean through lower centres as opposed to any indirect influence through the cortex cerebri.

[4] *loc. cit.*

experiments appearing to prove that one lateral half of the cerebellum controls the cortical cells of the opposite cerebral hemisphere. The probable paths by which such impulses pass have been traced, by the degeneration method, as far as the optic thalamus beyond which point they have not been traced upwards. In like manner, when considering the possibility that the effect is the result of the direct removal of a cerebellar influence from the muscles, no continuous paths along which such influences could travel can be traced by the degeneration method. It is true that Marchi[1] has traced degenerated fibres from the cerebellum to all the cranial nerves; but like Ferrier and Turner[2], I have been unable to confirm this observation. However, we are well aware that continuous paths are by no means necessary for the conduction of impulses, and that throughout the central nervous system the rule is that breaks occur in paths by the interposition of nerve cells at certain levels, so that as far as paths are concerned the effects may be quite well brought about either directly, or through the agency of the opposite cerebral hemisphere. That the effects are, however, not brought about through the agency, at any rate of the cells of the eye-area of the opposite cerebral hemisphere, is clear from the fact that when part of the eye-area of one cerebral hemisphere has been removed, and the opposite lateral lobe of the cerebellum is subsequently excised, the deviation of the eyeball consequent on the cerebellar lesion is practically the same as that met with when one lateral lobe of the cerebellum is removed in a dog whose cortical eye-areas are intact. This and other facts to be presently considered make it more probable that the abnormal position of the globes met with after ablation of parts of the cerebellum, is due to the taking off of some cerebellar influence directly exerted on the ocular muscles, rather than to any indirect effect brought about through the agency of the cortex of the opposite cerebral hemisphere. And that this direct effect is of a paralytic rather than irritative character, is put beyond question by the fact that after the eye has returned to its normal position it can be made to assume the abnormal position again under the influence of anæsthesia induced by ether. That a paralytic condition should show itself again under the influence of an anæsthetic, is easy of explanation; but that an irritation phenomenon should do so, is contrary to all we know of such conditions.

[1] Marchi. *Riv. Sper. d. Fren. e Med. Leg.* A. XII. 1886, F. I; A. XIII. 1887, F. IV; A. XVII. 1891.

[2] Ferrier and Turner. *Proc. Roy. Soc.* 1893, Vol. LIV. p. 476.

(*b*) *Nystagmus.* With regard to nystagmus the result of ablation of parts of the cerebellum, it is clear that we have to deal with two entirely different phenomena. The one is spontaneous and probably an irritation phenomenon, possibly reflexly induced; and the other is only evoked on voluntary movements of the globes, and is in all probability a paralytic phenomenon due to weakness of the muscles producing the movement of the eyes in any given direction, or due to weakness of the antagonists of these muscles.

The mechanism of the nystagmus which has been recovered from, and which reappears under the influence of an anæsthetic, is not easy to explain. It may be explained by supposing that had there been no cerebellar defect the eyes would have turned in a certain direction, but owing to the cerebellar defect they are inclined to turn in the directly opposite direction, and that as both influences are being simultaneously exercised on the globe nystagmus results. That is, first the one influence predominates, and then the other, in quick repeated succession, until the more powerful eventually prevails, and the globe is fixed in an abnormal position. Or it may be that there is a tendency for the eyes to turn in a certain direction, which is in keeping with their behaviour in normal dogs during narcosis, and that the cerebellar influence steadies the movement by acting antagonistically to it under normal circumstances, so that when it is wanting unsteadiness amounting to nystagmus results.

From either of these explanations it will be seen that I am inclined to class this form of nystagmus as a paralytic one, and not as an irritation phenomenon.

5. *Control experiments on the labyrinth and eighth nerve.*

The results of these control experiments make it clear that the effects obtained after ablation of parts of the cerebellum are in no way dependent on any interference with the labyrinth and eighth nerve. The operation on the cerebellum most likely to be attended with any of these labyrinthine structures is that in which one or other lateral lobe of that organ is removed. Now after ablation of one lateral lobe of the cerebellum the opposite eye is displaced downwards and outwards, whereas after lesions of the labyrinth and eighth nerve it is displaced inward, and according to Bechterew[1], also upward. The eye on the same side as the lesion we have seen returns to its normal position after

[1] *loc. cit.*

the effect of the anæsthetic has passed off, when the lesion is cerebellar, but when it is labyrinthine the ocular deviation persists; and even when the eye is in an abnormal position after ablation of the lateral lobe of the cerebellum, and before the effect of the anæsthetic has passed off, it is turned upwards and outwards, while after lesions of the labyrinth and eighth nerve it is turned downwards, and according to Bechterew also outwards. So too the nystagmus is of a totally different character in the two cases.

6. *The effects of removing one lateral lobe of the cerebellum and part of the eye-area of one cerebral hemisphere.*

The fact which appears to be best established by these experiments is that the influence exerted on the ocular muscles of the opposite eye, by one lateral lobe of the cerebellum and the cortical cells of the eye-area of the cerebral hemisphere on the same side as the lateral lobe of the cerebellum, antagonise each other. That is, while the one influence prevents the eye from being moved in one direction, the other prevents it from being moved in the exactly opposite direction, so that when either influence is lost separately, an abnormal position of the eyeball results, while when both are simultaneously removed, no such abnormal position of the globe is met with, its position being practically normal. Another way of stating the condition would be to say that one lateral lobe of the cerebellum and the opposite cerebral hemisphere exert a combined influence which tends to move the eye in one direction, while the other lateral lobe of the cerebellum and other cerebral hemisphere are responsible for an influence which tends to move the eye in an exactly opposite direction. These two influences antagonise each other; take away the whole of one, and the other predominates and causes the eye to assume an abnormal position; take away half of each, and the remaining halves antagonise each other. The last is the condition met with when part of the eye-area of one cerebral hemisphere and the lateral lobe of the cerebellum on the same side, are removed at the same time.

Another point which is made clear by these experiments is one that has already been discussed, viz. that the cerebellum exercises a perfectly independent action on the ocular muscles, its influence being a direct one, and not one brought about indirectly through the agency of the opposite cerebral hemisphere.

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FURTHER RESEARCHES ON EYE MOVEMENTS.

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I. Introductory Remarks.

In a former contribution to this *Journal*[1] in addition to other points dealt with I endeavoured to show that in the monkey division of the lateral recti responsible for turning the eyes to one side enabled me to differentiate with certainty the following movements on excitation of the frontal "eye-area" of one cerebral hemisphere. The movements of the eyes evoked under these circumstances were :—

[1] Vol. XVII. p. 1, 1894.

1. Simple direct upward movement.
2. Simple direct downward movement.
3. Combined movement upward and to the opposite side.
4. Combined movement downward and to the opposite side.
5. Convergence.

As was stated in that communication I made no attempt at precise localisation, but contented myself with demonstrating the possibility of evoking these separate movements on excitation of different foci in an area of the cortex from which formerly none but the simple lateral movement to the opposite side or the combined movements to the opposite side and upwards or to the opposite side and downwards, had been obtained.

At the time when I wrote that paper I was not aware of the existence of a paper by Professor Schäfer and Dr Mott[1] in which these observers state that faradization of the frontal "eye-area" in large specimens of Callithrix, one well-developed Bonnet and a large Rhoesus monkey showed "that as regards conjugate deviation of the eyes this area may be regarded as consisting of three zones, (1) a middle zone immediately below the horizontal part of the precentral sulcus, faradization of which is followed by simple lateral deviation, well-marked and without either upward or downward inclination; (2) an upper zone immediately above this, which may extend to and include part of the marginal gyrus, giving on faradization downward inclination, usually combined with lateral deviation; and (3) a lower zone immediately below the middle one, and sometimes extending nearly to the lower margin of the hemisphere, which gives upward inclination usually also combined with lateral deviation."

I am exceedingly sorry that I overlooked so important a paper on the subject I was dealing with; and I am anxious to take this opportunity of tendering my apologies to the authors of it.

As I find no mention made in the paper just alluded to that a separate focus was found excitation of which resulted in simple upward movement as distinct from another focus excitation of which was responsible for a combined upward and outward movement, or a focus for simple downward movement as distinct from another focus for the combined downward and outward movement, or a focus excitation of which resulted in convergence of the eyes, I conclude that these new points were established by the method of dividing the lateral recti muscles of the eyes before exciting the cerebral cortex.

[1] *Brain*, XIII. p. 165, 1890.

The object of the present short communication is to detail further results gained by the method of excluding the possibility of certain movements of the eyes taking place as a means whereby other movements not hitherto evoked can nevertheless be shown to be represented in the cerebral cortex in close proximity to the movement which has been excluded. In order that the method should be put to a searching test I have employed dogs and cats, animals lower in the scale, and whose cortical centres are less differentiated than those in the monkey.

A further point dealt with on the present occasion is the position which the eyes assume during general convulsions in dogs and cats in whom the "eye-area" has been removed from one cerebral hemisphere, or in whom one lateral half of the cerebellum has been extirpated. The position of the eyes under such circumstances is contrasted with their position during general convulsions in dogs and cats whose central and peripheral nervous systems are intact.

II. **Plan of Procedure.**

Ether narcosis was induced at the commencement and continued throughout the course of the experiment in each instance. The anterior portion of the cerebral hemisphere was exposed on one side ; sometimes on its external surface only, while at other times its orbital surface was also exposed. In the latter instance the opposite eyeball was alone available for subsequent observation owing to the interference with the natural support of that on the same side.

In those instances in which electrical excitation was employed the induced current was directed to the "eye-area" so as to ascertain what movement of the eyes resulted in each instance. The next step was to divide the external rectus of the opposite eye alone, or that muscle together with the internal rectus of the eye on the same side as the cerebral hemisphere under investigation.

In the ablation experiments an incision was made into the cerebral hemisphere transversely in the line of the crucial sulcus or a little posterior to this, and the whole of the anterior part of the hemisphere in front of this incision was extirpated.

When one lateral half of the cerebellum was extirpated the method of procedure was that adopted in my former experiments, and detailed in the paper already alluded to[1].

[1] *loc. cit.*

Electrical excitation was carried out by means of fine platinum-pointed electrodes about 2 mm. apart, connected with the secondary coil of a du Bois Reymond's inductorium, supplied by a single bichromate cell.

General convulsions were induced by the injection of a varying quantity of the essential oil of absinthe into the external jugular vein on one side.

III. Ocular movements represented in the cerebral hemispheres of the dog and cat.

Dogs. Excitation of the "eye-area" of the frontal region of the cerebral hemisphere of the dog results in turning of both eyes to the opposite side, as is well known, but neither by variation of the strength of the induced current used, nor of the depth of narcosis, have I been able to evoke from this same area any other ocular movement but that of turning of the eyes to the opposite side from the cerebral hemisphere stimulated, so long as all the ocular muscles be intact. If however the external rectus of the opposite eye and the internal rectus of the eye on the side of the cerebral hemisphere under investigation be divided, then this lateral movement of the globes to the opposite side no longer takes place on excitation of the "eye-area," the eyes moving in quite a different direction instead. The direction in which the eyes now invariably move is directly upwards without any trace of lateral inclination.

In some instances instead of dividing both the external rectus of the opposite eye and the internal rectus of that on the same side as the hemisphere excited, the former muscle was alone divided. This procedure was well adapted for contrasting the movements of the eye whose external rectus was divided with that all of whose muscles were intact, for when the "eye-area" was stimulated under these circumstances the eye on the same side moved inwards, that is to the opposite side, while the opposite eye moved distinctly upwards, without any lateral inclination.

Contrary to my experience in the monkey, I was unable to find any focus in the frontal region of the hemisphere of the dog which would give any but the upward movement after the lateral recti responsible for turning the eyes to the opposite side had been divided. In consequence of this I next proceeded to eliminate in great measure the upward movement by division of the superior rectus, but this was

followed by so much downward rotation of the globe, possibly by the tonus of the inferior rectus chiefly, that it was found impossible to evoke any movement of the globe or globes on excitation of the cortical "eye-area." Not even any trace of internal movement of the opposite eye could be detected.

At Professor Horsley's suggestion this downward rotation of the globes was rectified by connecting a piece of very delicate indiarubber band to the peripheral stump of the divided superior rectus and making sufficient traction on it to raise the eye to about its normal position. Under these circumstances excitation of the frontal "eye-area" resulted in two more movements of the eyes being evoked; a simple downward movement and a movement of the opposite eye inwards, i.e. towards the side of the hemisphere stimulated.

Cats. What has been said of the dog holds true in the cat also. Excitation of the frontal "eye-area" of one cerebral hemisphere results in turning of the eyes to the opposite side. Excitation of the same area of the cortex after section of the external rectus of the opposite eye and the internal rectus of the eye on the side of the hemisphere under observation results in upward movement of both globes. Division of the external rectus of the opposite eye alone, allows ot the movement of this eye being contrasted with that of the eye whose muscles are all intact, and whereas the intact globe moves inward, that is to the opposite side, that on the opposite side moves upwards.

As in the dog, no other ocular movement could be evoked on cortical excitation with the lateral recti alone divided, and section of the superior rectus in conjunction with the lateral resulted in so much downward rotation of the globe, or globes, that it was impossible to evoke any further downward rotation on cortical excitation, nor was there any evidence of turning of the opposite eye inwards, that is towards the hemisphere stimulated.

Each eye was raised from its abnormal position of downward displacement by means of a delicate indiarubber band attached to the stump of the superior rectus, as in the case of the dog, and as in that animal excitation of the frontal "eye-area" evoked simple downward movement, and turning of the opposite eye inwards, that is towards the side of the hemisphere excited.

IV. Position of the eyes during general convulsions in dogs and cats whose central and peripheral nervous systems are intact.

Dogs. With the exception of a very slight displacement of both eyes *downwards and a little inwards* no alteration could be detected in the position of the eyes during general convulsions the result of intravenous injections of absinthe, in dogs whose central and peripheral nervous systems were intact. The very slight downward and inward displacement was quickly recovered after the general convulsions ceased. At no time during the convulsions was there any lateral displacement of the eyes other than the very slight inward inclination of both already alluded to.

Cats. Slight as was the displacement of the eyes of dogs whose central and peripheral nervous systems were intact, the displacement of the globes was still less evident in normal cats during general convulsions evoked by absinthe, though in direction it was the same as in the case of dogs; that is the eyes were directed very slightly *downwards and inwards.* It is by no means easy to be too certain of the amount of upward or downward displacement of the eyes during convulsions, as the eyelids are sometimes spasmodically closed during the convulsions, while at other times they are wide open.

V. Position of the eyes during general convulsions in dogs and cats whose "eye-area" in one cerebral hemisphere has been extirpated.

In my former paper[1] it was shown that the immediate effect of extirpation of the frontal "eye-area" in one cerebral hemisphere was turning of both globes towards the damaged hemisphere, and that after a variable time the eyes once more assumed their normal positions, but that it was then possible to re-establish the abnormal position of the globes in a certain stage of ether narcosis. The present research deals with the question in a different manner, for having excluded the influence of the cortex of the frontal "eye-area" of one cerebral hemisphere, all other centres governing eye movements are excited to exaggerated action.

The whole frontal region of one cerebral hemisphere including the "eye-area" was removed on one side, after which the position of the eyes

[1] *loc. cit.*

was carefully observed. Their precise position varied with the depth of ether narcosis, therefore it was necessary to keep the animal in as nearly as possible the same stage of ether narcosis while the observations were being made. Having satisfied myself as to the real position of the globes, the external jugular vein was exposed on one side of the neck and 2, 3 or 4 minims of the essential oil of absinthe were injected into the vein in the direction of the blood stream. During the general convulsions which followed this procedure the position assumed by the animal's eyes was as follows:—

Dogs. In dogs, if the stage of ether narcosis was such that there was inclination of the eyes towards the hemisphere whose frontal region had been removed, this inclination was in rare instances intensified during the first general convulsions which resulted. The usual position which the eyes assumed in all subsequent convulsions, and in the majority of instances even in the first convulsion, was one in which both eyes were directed downwards and inwards to a considerably greater extent than in dogs whose central and peripheral nervous systems were intact.

Sometimes, owing to the operation for exposure of the frontal region of the cerebral hemisphere having interfered with the posterior wall of the orbit, the opposite eye was alone available for observation. The position which it assumed during the convulsions was invariably one of downward and inward rotation, that is towards the side of the damaged hemisphere.

Cats. When the frontal region of one cerebral hemisphere including the "eye-area" is excised in cats, and absinthe subsequently administered by intra-venous injection, the general convulsions which result are attended with displacement of the eyes from their normal position to a much smaller extent than in dogs, but the direction of displacement is the same, viz. downwards and inwards of both eyes. This displacement is greater than in normal cats in whom, as has been seen, the displacement of the eyes is extremely trivial.

VI. Position of the eyes during general convulsions in dogs and cats in whom ablation of one lateral half of the cerebellum has been practised.

Dogs. According to Luciani, ablation of one lateral half of the cerebellum results in deviation of both eyes to the opposite side. My own experiments, in which one lateral half of the cerebellum was

removed in dogs, confirmed this observation in so far as the displacement of the opposite eye was concerned, though I could detect little or no displacement of the eye on the same side (as the lesion) in the same direction as its fellow. Further, I found that in animals whose eyes had recovered their normal positions some time after the operation, the displacement could be reproduced by inducing ether narcosis, the displacement resulting at a given stage of the anæsthesia.

Such results as these would appear to warrant our expecting to find similar displacements of the eyes, though to a greater degree, when the intact nerve centres which govern their movements are excited to discharge, in an animal whose one lateral half of the cerebellum has been removed, before the administration of absinthe. Contrary to such expectations, it was found that the displacement of the globes was as a rule such that the eye on the side of the lesion was directed downwards and inwards, while the opposite eye was also directed downwards and inwards. In other words the direction of displacement was the same as in normal dogs and the degree of displacement about the same as in dogs in whom the frontal region of one cerebral hemisphere had been removed, or possibly a little less.

On rare occasions both eyes were directed to the side of the lesion and downwards during the first convulsions; but the usual displacement of the globes met with was that already described.

Cats. A moderate amount of inward rotation of both eyes with a slight downward inclination was the position which the globes assumed during general convulsions in cats in whom one lateral half of the cerebellum had been removed. Thus the position of the eyes in these animals was the same as that of dogs under similar circumstances; but the amount of obvious displacement of the globes was smaller in amount in cats than in dogs.

VII. Concluding Remarks.

1. Ocular movements represented in the cerebral hemispheres of the dog and cat.

Better proof of the value of the method of excluding one movement before attempting to elicit others whose centres are closely related in the cerebral cortex to those of the movement excluded could not be had than that furnished by the results of excitation of the frontal "eye-area" of the cerebral cortex of the dog and cat after division of the lateral

recti muscles which normally turn the eyes away from the hemisphere excited.

So far as I am aware, no one has been able to evoke any other but the lateral movement of both eyes to the opposite side on exciting the frontal "eye-area" of the dog and cat. And I have certainly not been able to evoke any other movement of the globes in these animals, so long as the lateral recti responsible for turning the eyes away from the hemisphere excited are intact. But directly this lateral movement was excluded by division of the lateral recti which bring it about, excitation of the same region of the cerebral cortex resulted in unmistakable simple upward movement of the eyes, a movement no trace of which could be detected when the same cortical area was most carefully explored with the lateral muscles of the eyes intact. So too, on further dividing the superior rectus it has been possible to evoke the simple downward movement and movement of the opposite eye inwards.

In view of such evidence it cannot well be denied that it is possible for one movement to be so powerfully represented in the cerebral cortex as to make it impossible to evoke other movements whose cortical centres are close to it, but which have not so powerful a representation, as has been advocated by Dr Hughlings Jackson. In the instance under consideration it is reasonable to suppose that the upward movement of the eyes is so much less represented in the cerebral cortex than is the lateral movement to the opposite side that no electrical stimulus can be so regulated as to be at once strong enough to evoke the upward movement, and weak enough not to evoke the lateral movement. To make my meaning clearer it is possible to conceive that the chief focus for the upward movement is situated in the cortex close to the chief focus for the lateral movement, but that the peripheral region of the lateral focus overlaps the chief focus for the upward movement and that the representation of the lateral movement even in this peripheral portion of its area of representation is more powerful than is the upward movement at its chief focus of cortical representation; so that excitation of the chief focus for the upward movement results not in that movement but in one which overpowers it, viz. the lateral movement whose representation overlaps the chief focus for the upward movement and is at that point even more powerful a representation than is the representation of the upward movement.

It is interesting to compare the results obtained in the dog and cat

with those formerly obtained in the monkey[1]; for in the monkey after the lateral movements of the eyes to the opposite side were excluded, the foci for several other movements of the globes could be demonstrated in the frontal "eye-area," whereas in the dog and cat the upward movement could alone be evoked as long as the superior rectus was intact. This is important as pointing to the probability that the upward movement of the eyes is, at any rate in these animals, of next importance to the lateral movements, and that after the lateral movements it is the next most powerfully represented in the cerebral cortex.

2. Position of the Eyes during Convulsions.

Inasmuch as the eyes turn to a varying extent to one side at a given stage of ether narcosis in normal dogs, it might have been expected that evidence of the same inequality of representation on the two sides might have been forthcoming during the convulsions evoked by absinthe, instead of which, as has been seen, no conjugate lateral displacement of the eyes resulted under these circumstances, the only obvious displacement met with being exceedingly slight and of an entirely different character.

So too the results which attended the general convulsions in dogs and cats, in whom the "eye-area" had been excised from one cerebral hemisphere, were not what might have been expected on the assumption that the convulsions evoked by absinthe are mainly of cortical origin. In a purely cortical discharge, inasmuch as the cortical centres concerned with moving the eyes to one side had been destroyed, it would have been reasonable to suppose that the eyes would have been displaced laterally in the opposite direction by the discharge of energy from the cells of the "eye-area" of the intact hemisphere; a result which was only met with under the most exceptional circumstances, and then only in the first of a series of convulsions in the same animal.

No less contradictory are the results which were obtained when general convulsions were evoked in dogs and cats in whom one lateral half of the cerebellum had been extirpated. Two possibilities seemed equally open under these circumstances; either that the displacement of the eyes which results from such a cerebellar lesion would be maintained or intensified during the general convulsions, or that inasmuch as such a lesion of the cerebellum induces an inequality in the

[1] *loc. cit.*

excitability of the two cerebral hemispheres in which that on the opposite side from the cerebellar lesion is the more excitable[1], the eyes might have both been turned towards the side from which the lateral half of the cerebellum had been removed. The former of these results was never met with, and the latter was of the rarest, and then only in the first convulsions of an animal who had a series of convulsions. The actual displacement of the eyes which was met with in the large majority of instances was similar to that met with during convulsions in normal dogs and cats, or in dogs and cats in whom the frontal "eye-area" of one cerebral hemisphere had been removed; the only difference being one of degree, the animals with the cerebellar lesion showing an amount of displacement intermediate in degree between that met with in normal dogs and cats, and that in these animals in whom the "eye-area" of one cerebral hemisphere had been excised, in which latter the displacement appeared to be greatest.

Not the least curious of the results obtained was the tendency to downward displacement of the globes to a varying extent during the convulsions in all the animals. Had this been met with only in the animals in whom one lateral half of the cerebellum had been removed it would not have been surprising, for a certain amount of downward rotation, at any rate in the opposite eye, is characteristic of such a lesion quite apart from any convulsions. But that this tendency to downward displacement of the globes should also be met with during convulsions in normal animals and in those in whom the "eye-area" from one cerebral hemisphere has been removed, is a fact which cannot be passed over without comment. The results of electrical excitation of the cortex, both in the cat and dog, after division of the lateral muscles of the eyes, have shown that probably the movement of the eyes represented next in degree to the lateral movement is the upward movement. Now under these circumstances it is clear that in convulsions of purely cortical origin if the eyes are displaced at all vertically they ought to be displaced upward and not downward.

These various considerations make it fairly evident that the displacement of the eyes met with during convulsions under the circumstances that have been detailed can only be explained by supposing that they depend on discharges from centres in the cerebral cortex other than those of the frontal "eye-area," or that they are brought about by the action of nerve centres situated in some region of the

[1] *Phil. Trans. Roy. Soc.* Vol. CLXXXV. p. 819, 1894.

central nervous system other than the cerebral cortex or the cerebellum. And it would also appear that, as far as the eye movements are concerned, absinthe is capable of evoking discharges from these centres, wherever they may be situated, which overpower the effects of any discharges evoked by the drug either from the frontal "eye-area" of the cerebral hemisphere or from the cerebellum.

In conclusion I wish to thank Professor Victor Horsley for allowing me to carry out the investigations, which form the subject of this paper, at the Pathological Laboratory of University College.

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"The Influence of Intra-Venous Injection of Sugar on the Gases of the Blood."

By VAUGHAN HARLEY, M.D., Teacher of Chemical Pathology, University College, London, Grocer Research Scholar. Communicated by GEORGE HARLEY, M.D., F.R.S. Received May 9, 1894.

In a paper on "The Effects and Chemical Changes of Sugar injected into a Vein"* I showed that when grape sugar is injected

* 'Roy. Soc. Proc.,' 1893.

into the jugular vein of a dog it causes an augmentation in the quantity of lactic acid in the circulation, the quantity of the acid steadily increasing until it reaches its maximum in about three hours after the injection. It then gradually, hour by hour, decreases, until in about six hours it returns to the normal amount. The question as to the base with which the lactic acid combines to form a lactate is, however, still unsettled.

The results of Walter's* experiments, in conjunction with the often-noticed fact that ammonia is increased in the urine of diabetes, led me to imagine that the lactic acid combined with ammonia, until I found that the breaking up of sugar in the organism has no influence whatsoever on the amount of ammonia in the blood, and consequently it cannot be the base.

It then appeared to me probable that the lactic acid had combined with the bases of carbonates in the blood, having driven out the carbonic acid from its compound.

In order to try and settle this point, I estimated the quantity of carbonic acid in the blood under different conditions.

The series of experiments I am now about to record were performed in the Physiological Institute at Leipzig, and I wish to express my gratitude to Professor C. Ludwig for the kind assistance he gave me in the matter.

The experiments, which were made on dogs, were conducted in the same manner as in my previous researches, above alluded to, except that blood was withdrawn only three times from each dog. In order to obtain a normal standard, the first specimen of blood was taken before the sugar was injected, the second was withdrawn in an hour, and the third in from three to five hours after the intra-venous injection of the sugar.

In order that the composition of the blood might be altered as little as possible by the bleeding, only 30 c.c. of blood was collected each time.

In all cases the blood was collected under mercury from the carotid artery. The gases were pumped from the blood by means of a Ludwig mercurial pump, and analysed by Bunsen's method.

The quantities of gases found were calculated at 0° C. and 760 mm. of mercury, and are expressed in volumes per cent.

Before alluding to the changes found in the blood gases, I will briefly give, in a tabular form, the results obtained from each experiment:—

* Walter, 'Arch. Exper. Path. u. Pharm.,' vol. 7, p. 158, 1877.

Experiment 1.

Weight of animal.	Condition.	Quantity injected of			Volumes per cent. at 0° C. and 760 mm. Hg.	
		Sugar, in grams.		NaCl solution.	Carbonic acid.	Oxygen.
kilos. 7		total.	per kilo.	c.c.		
	Before sugar injection ...	60	8·56	120	37·380	22·280
	1 hour after ..	..	..	..	27·006	17·071
	5 hours after..	..	..	..	34·357	14·886

The only nerve symptoms after the sugar injection were manifested in vomiting and muscular tremors. These were not accompanied by coma or any other symptom.

The quantity of carbonic acid found in the standard specimen of blood was 37·380 per cent., whereas, in that taken an hour after the sugar injection it was only 27·006 per cent., that is to say, a diminution of 10·374 per cent. in the amount of carbonic acid followed upon the intra-venous injection of the sugar, while the blood withdrawn five hours later contained 34·357 per cent. of carbonic acid, this being only 3·023 per cent. less than that in the standard blood. The carbonic acid, thus tending to return to the normal amount, showed that the influence of the sugar on the carbonic acid in the blood is merely temporary.

The quantity of oxygen in the standard blood was found to be 22·280 per cent. An hour after the sugar injection it had fallen to 17·071 per cent., thus giving a diminution of 5·209 per cent. Five hours later it was still further decreased, being only 14·886 per cent. Consequently, in this respect the effect of the sugar on the oxygen is different from that upon the carbonic acid.

Experiment 2.

Weight of animal.	Condition.	Quantity injected of			Volumes per cent. in 0° C. and 760 mm. Hg.	
		Sugar, in grams.		NaCl solution.	Carbonic acid.	Oxygen.
kilos. 5		total.	per kilo.	c.c.		
	Before sugar injection ...	50	10	100	38·541	19·902
	1 hour after ..	..	..	..	28·042	7·220
	4½ hours after.	..	..	..	28·926	13·968

The nerve symptoms following the injection of the sugar were greater in this case. The vomiting and tremors of the limbs were followed by well-marked epileptic fits, which, an hour later, were succeeded by a semi-comatose condition. Although the animal could still be roused, it remained in a sleepy condition up to the third bleeding, when it was killed.

The percentage of carbonic acid fell in the first hour after the sugar injection, while the animal was in a drowsy condition, from 38·541 to 28·042. This gives a diminution of carbonic acid of 10·499 per cent. Four and a half hours after the injection the carbonic acid had risen to 28·926 per cent. That is to say, it was 9·615 per cent. less than the quantity found in the standard blood.

The oxygen which originally stood at 19·902 per cent. fell, in the first hour, to 7·220 per cent.; therefore it was 12·682 per cent. less than the normal amount. In four and a half hours after the sugar injection it increased to 13·968 per cent., which is only 5·934 per cent. less than the original quantity found.

Thus it appears in this case there was a greater diminution in both the carbonic acid and oxygen of the blood during the first hour than in the former experiment; a result corresponding with the far greater nerve disturbances, and no doubt due, as stated in my former paper, to a larger percentage of sugar to bodily weight having been injected into the circulation. It was found in this case that the carbonic acid was, four and a half hours after the injection of the sugar, while the animal was in a semi-comatose state, almost as low as during the first hour. The oxygen had by this time, on the other hand, markedly increased in quantity.

These results having been obtained, it was decided to withdraw the third portion of blood somewhat earlier after the sugar injection than in the foregoing cases.

Experiment 3.

Weight of animal.	Condition.	Quantity injected of			Volumes per cent. at 0° C. and 760 mm. Hg.	
		Sugar, in grams.		NaCl solution.	Carbonic acid.	Oxygen.
kilos.		total.	per kilo.	c.c.		
3	Before sugar injection. ..	240	10·435	480	42·260	
	1 hour after ..	..	..	..	33·075	10·217
	3 hours after..	..	..	..	38·000	14·569

Here the nervous symptoms which showed themselves in the form of vomiting, trembling, and two epileptic attacks were followed by

drowsiness, which lasted until after the second bleeding. The drowsiness in this case passed off before the third bleeding.

In the standard specimen of blood the carbonic acid was 42·260 per cent., and an hour after the intra-venous injection of the sugar it fell to 33·075 per cent., being a decrease of 9·185 per cent. The third portion of blood taken in three hours, that is to say after the drowsiness had passed off, was found to contain 38·000 per cent. of carbonic acid, a decrease from the normal of 4·260 per cent.

The specimen of oxygen from the normal blood was lost. The quantity found an hour after was 10·217 per cent., and three hours after the sugar injection it had increased to 14·569 per cent.

The results of this experiment, as far as they go, correspond very closely with those of Experiment 1; in which there was likewise only a very slight nervous disturbance.

Experiment 4.

Weight of animal.	Condition.	Quantity injected of			Volumes per cent. at 0° C. and 760 mm. Hg.	
		Sugar, in grams.		NaCl solution.	Carbonic acid.	Oxygen.
kilos.		total.	per kilo.	c.c.		
20·5	Before sugar injection....	230	11.2	460	39·520	16·025
	1 hour after ..	..	..	..	32·140	15·561
	3 hours after..	..	..	..	24·725	17·767

Although this dog had vomiting and marked tremor of the limbs there were no epileptic seizures. Sleepiness, however, came on later, and was marked at the time of the third bleeding.

In the first specimen of blood the quantity of carbonic acid was 39·520 per cent., and it diminished during the first hour after the sugar injection to 32·140 per cent., being a decrease of 7·380 per cent. Three hours after the injection of the sugar, the carbonic acid fell still further, it being then only 27·725 per cent., that is to say 14·795 per cent. less than the original amount.

The oxygen, which at the beginning was 16·025 per cent., decreased during the first hour to 15·561 per cent., being a loss of 0·464 per cent. By the third hour it again rose to 17·767 per cent., that being 1·742 per cent. more than was found in the normal blood.

As in Experiment 2, this dog had become semi-comatose by the third bleeding, the carbonic acid being then even less than what it was during the first hour.

Having now briefly given the results met with in each separate experiment, I will now consider the results as a whole.

In the first place, we see there was a decrease in the quantity of carbonic acid in all the different specimens of blood during the first hour after the sugar was injected, the diminutions being 10·374, 10·499, 9·185, and 7·380 per cent.

In the second place, the blood, taken five hours after the sugar was injected, showed a decrease of 3·023 and 9·615 per cent. (in Experiments 1 and 2); while after three hours there was a decrease of 4·260 per cent. (in Experiment 3). In all the three cases it had therefore shown, during the later hours, a more or less marked tendency to return to the normal amount. In Experiment 4 the blood at the third hour contained 14·795 per cent. less carbonic acid than the normal blood, and 4·415 per cent. less than what it contained at the first hour. This discrepancy may be due to the fact that a greater percentage of sugar was injected, and the dog was in consequence rendered more comatose. This view seems the more likely, as in Experiment 2, when the dog was semi-comatose, the carbonic acid was markedly diminished at the fifth hour.*

These united results support the view that the lactic acid derived from the splitting up of the sugar in the animal body drives off the carbonic acid from the sodium salts and replaces it. This view is still further supported by the fact that the quantity of carbonic acid in the blood withdrawn at the different periods after the sugar injection, varied in the same manner as the quantity of lactic acid had been found to do. In both cases during the first hour after the sugar injection, one finds larger quantities than during the later hours.

Whether the percentage decrease in the amount of the carbonic acid hinders its elimination by the lungs or not will depend upon how much power the combined lactic acid has of hindering the blood from taking up the carbonic acid from the tissues and the tension of the existing gas.

This point would be ascertained by estimating the quantity of carbonic acid expired after the sugar injection. The experiments I have already published† on this point show that there is no decrease in the amount of carbonic acid expired from an animal immediately after sugar has been injected into its circulation. In fact there was an actual increase of carbonic acid in all but one case‡ during the first hour.

* "Small dogs," as I stated in my former paper, "are relatively much more susceptible than large ones to the effect of sugar injection."

† Vaughan Harley, "Influence of Sugar in the Circulation on the Respiratory Gases," 'Journal of Physiol.,' vol. 15, p. 139, 1893.

‡ *Ibid.*, Exp. 9, p. 147.

There was a marked decrease of carbonic acid during the later hours in those cases which suffered from coma.

It would thus seem that in those cases when there are no nervous symptoms caused by the intra-venous injection of sugar, while the quantity of lactic acid is at its highest and the quantity of carbonic acid in the blood is at its lowest, more carbonic acid is expired than before the injection of the sugar.

An explanation to this fact, if it really exists, is at the present moment impossible. In order to settle this point it would be necessary in the same animal to make all the analyses at the same time; which would be impossible without an exceptionally large dog, as the quantity of blood needed would cause of itself changes in the metabolism.

In the next place the changes met with in the quantity of oxygen in the blood are still more surprising, as there is no known reason why hæmoglobin should not take up the usual amount of oxygen as it does in health after the intra-venous injection of sugar.

In all of the experiments the quantity of oxygen is seen to have been markedly diminished during the first hour after the sugar injection.

In three of them it fell 0·464, 3·209, and 12·682 per cent. below the normal standard during the first hour. This result can be partially explained by the influence of the endosmotic flow of the juices of the tissues into the circulating blood, which is known to occur when the quantity of sugar in the blood is increased. For in a series of similar experiments Brasol* found that during the first five minutes after the injection of sugar the proteids of the serum were reduced to even below one half of their previous amount, while one or two hours after the injection the proteids had, as a rule, returned to the normal amount.

During the third and fifth hours after the sugar injection it will be noticed that the quantity of oxygen in the arterial blood was 14·886, 13·968, 14·569, and 17·767 per cent.; that is to say the quantity that is usually found in venous blood.

The diminution in the quantity of oxygen, even from three to five hours after the sugar injection, cannot therefore be explained on a dilution theory.

* Brasol. Du Bois-Reymond's 'Archiv.,' 1884.

Harrison and Sons, Printers in Ordinary to Her Majesty, St. Martin's Lane.

[*From the Journal of Physiology. Vol. XVIII. No.* 1, 1895.]

THE NORMAL ABSORPTION OF FAT, AND THE EFFECT OF EXTIRPATION OF THE PANCREAS ON IT.

By VAUGHAN HARLEY, M.D., *Assistant Professor of Pathology and Teacher of Chemical Pathology at University College, London. Grocer Research Scholar.*

The results recorded by previous observers on the absorption of fat from the alimentary canal are so different, that I considered it would be well in connection with pancreatic diabetes, after total extirpation of the pancreas, to take up this subject. To properly understand this, however, I found it necessary to make a series of experiments on the normal absorption of fat, and the results of these experiments I shall first narrate, as they will serve as a standard of comparison to the experiments after extirpation of the pancreas.

Eberle[1] showed that a watery infusion of the pancreas when shaken up produced an emulsion, from which he considered that the function of the pancreatic juice was to emulsify the fat in the intestine, and thus aid absorption.

Cl. Bernard[2] (to whom the credit is usually given of having made the discovery) still further investigated this action of pancreatic juice on fats, and he considered that they could not be absorbed by the lacteals without first being split up into fat acids and glycerine by a pancreatic ferment.

Bidder and Schmidt[3] pointed out that the presence of acids prevented the pancreatic juice breaking up neutral fats, which results Grutzner[4] confirmed.

Bunge[5] considered that the fats are emulsified by the pancreatic juice splitting up some of the neutral fats into glycerine and fatty acids, and alkaline carbonate in the intestines then forming soaps with the fat acids set free.

[1] Eberle. Quoted by Gamgee, *Physiological Chemistry of the Animal Body*, Vol. II. p. 210, 1893.

[2] C. Bernard. *Leçons de Physiol. expérimentale*, Vol. II. p. 178.

[3] Bidder and Schmidt. *Die Verdauungssäfte*, p. 250.

[4] Grützner. "Notizen über einige ungeformte Fermente des Säugethierorganismus." *Pflüger's Archiv*, XII. 302, 1876.

[5] Bunge. *Lehrbuch der physiologischen Chemie*, 2nd ed. p. 175, 1889.

If fat containing some fat acids be shaken up with carbonate of soda in a test tube, a soapy solution is formed, in which the neutral fat is in a sort of fine emulsion; but that this is not the method followed in the intestines was shown by Cash[1], who, while working in C. Ludwig's Laboratory, found that in dogs the intestinal contents are always acid and in no cases did the fat exist in the form of an emulsion. I have frequently confirmed the fact of the contents of the intestines being acid. I first noticed it in 1889, working in C. Ludwig's Laboratory, and it was on my calling Prof. Ludwig's attention to it that he referred me to the work of Cash. That the contents of a dog's intestines should always be acid is a point of so much importance that I here give the results of a series of experiments made on different animals, and with varied diet. The contents of each part of the alimentary canal was first well mixed before testing.

TABLE 1. *On reaction of the alimentary tract in dogs, cats and rabbits on various diets.*

Animal	Kind of diet	Time after last meal. Hours	Reaction			
				Small intestine		
			Stomach	Upper half	Lower half	Large intestine
Dog	4 days fast, and then milk	3	acid	faintly acid	markedly acid	markedly acid
,,	,,	7	acid	faintly acid	acid	acid
,,	,,	18	faint alkaline	faintly acid	faint acid	acid
,,	meat over a week	6	acid	faintly acid	acid	acid
,,	,,	10	acid	acid	acid	acid
,,	biscuits	6	acid	faintly acid	acid	markedly acid
Cat	meat	6	acid	faintly acid	acid	acid
Rabbit	greens	—	acid	faintly acid	markedly acid	acid
,,	oats	—	acid	markedly acid	markedly acid	acid

[1] Cash. "Ueber den Antheil des Magens und des Pankreas an der Verdauung des Fettes." *Du Bois Reymond's Arch.* 1880, p. 323.

In the preceding table it is seen that the contents of the intestines are acid not only on a flesh or milk diet, but also on a farinaceous one of biscuits. In only one case in which the dog was killed eighteen hours after food was any part of the alimentary canal found alkaline, and in this case the stomach reacted faintly so to litmus paper. This exception no doubt was due to the dog having swallowed some saliva immediately before being killed. It is further seen that both in cats and rabbits, the reaction of the intestines is in all cases acid.

Gamgee[1] draws attention to the error of speaking of an alkaline intestine in the various text-books of physiology. The acid reaction of the intestinal contents is no doubt due to lactic acid which has been there formed, and neutralised the sodium carbonate present; the excess of lactic acid present gives rise to the acid reaction.

It is impossible even to mention in a paper like this the varied opinions on the cause and mechanism by means of which fat is rendered capable of passing through the mucous membrane of the intestines; merely recapitulating the literature of the subject alone would take up too much space. In a few words we may say that it has generally been supposed that the first step in the process is the splitting up of some of the neutral fat into fat acids and glycerine by means of pancreatic juice. That the pancreas alone possesses this power was long ago shown to be an error, for in 1858 Marcet[2] showed that this may occur even in the stomach. Cash[3] pointed out that a ferment could be extracted from the dead stomach which had this action, while Ogata[4] still further under C. Ludwig's direction showed that the same thing occurred in the living stomach of a dog. From these experiments it is seen that the pancreas is not the sole organ which yields a secretion capable of splitting up neutral fat; consequently one must imagine that even if the pancreatic juice were absent, this so-called first stage in the emulsification of fat in the intestines would still take place.

With these few remarks I shall proceed to describe the method of procedure employed in the experiments about to be narrated.

Method of procedure:

In all cases the dogs were kept fasting for two days, and the bowels daily washed out with an enema of hot water, and after, a small glycerine enema was given in order to help the expulsion of the water employed. In those cases in which the pancreas was to be extirpated

[1] Gamgee. *loc. cit.* p. 446.
[2] Marcet. *Medical Times and Gazette*, XVII. 210.
[3] Cash. *loc. cit.* [4] Ogata. *Du Bois Reymond's Arch.* 1881. 515.

this was done on the third day. The entire gland was removed under an anæsthetic, and afterwards the animal kept perfectly quiet. On the fourth and fifth mornings the bowels were again washed out as before in order to remove any fæces which might be in the lower bowel so as to get a comparatively empty intestine. The washing out after the pancreas was removed had the further advantage of removing any pancreatic secretion that might have accidentally remained in the intestine. The normal dogs had the same washing out processes performed on them up to the fifth day. Each animal was then given a measured quantity of warm milk, and after a certain number of hours they were killed by means of chloroform.

The entire contents of the stomach, small and large intestines were separately collected and analysed. A specimen of the milk given was also analysed.

The paper will be divided into two parts:

Firstly. The Normal Absorption of Milk Fat.

Secondly. The Absorption of Milk Fat after Extirpation of the Pancreas.

The Normal Absorption of Milk Fat.

It is as well to express the results of the experiments in a tabular form, as the citing of each separate experiment would render this paper unnecessarily bulky.

TABLE 2. *Showing the normal absorption of milk fat in dogs. The quantity of fat as given in grams.*

No. of Exp.	Weight of dog in kilos	Time of digestion. Hours	Total fat given	Fat remaining in			Total fat remaining	Total fat absorbed
				Stomach	Small intestine	Large intestine		
1	7·824	3	9·872	5·488	2·032	0·319	7·839	2·033
2	7·256	4	12·505	9·321	0·782	1·207	11·310	1·195
3	7·940	7	10·799	4·866	0·923	0·634	6·423	4·376
4	12·825	7	22·806	12·970	0·977	0·402	14·349	8·457
5	6·858	7	9·471	3·503	0·845	0·791	5·139	4·332
6	10·350	7	12·027	8·116	0·623	0·740	9·479	2·548
7	8·503	18	15·148	0·000	0·970	1·181	2·161	12·987

In the above table it is seen in Exp. 1 and 2, the quantity of fat remaining in the stomach varies very considerably, for in Exp. 1, after three hours, out of 9·872 grams only 5·488 grams remained in the stomach, while in Exp. 2, 12·505 grams were given, and there remained

9·321 grams. In the intestine the difference is even more marked. In Exp. 2, the large intestine probably yielded a larger amount of fat than it ought to have done, as there was some dark fæcal matter in the cæcum which had not been removed by the enema, and this was analysed along with the fresh contents. The dogs that had digested during seven hours (Exp. 3, 4, 5, 6) showed also much variation in the quantity of food remaining in the stomach, while the quantities in the small and larger intestines resembled each other much more closely. In Exp. 7, the stomach was empty eighteen hours after feeding, while the quantity of fat in the small intestine corresponded with that found in the other experiments after seven hours. The quantity of fat in the large intestine is, however, larger than in any of the other experiments (except Exp. 2). This can be accounted for by the time that had elapsed since the taking of food having allowed it to pass down the alimentary canal and from thence to be absorbed, while that which was remaining in the large intestines would represent fæces. In all probability some of this would have been absorbed before the stool was discharged, as the lymphatics were found at the autopsy still well filled with chyle.

In order better to compare the results obtained in the above table, the following shows the fat in proportion to the normal weight per kilo.

TABLE 3. *Normal absorption of milk fat per kilo of animal weight.*

No. of Exp.	Weight in kilos	Time of digestion. Hours	Total fat given	Fat remaining in			Total fat left	Absorbed	Absorbed p. c.	Left p. c.
				Stomach	Small intestine	Large intestine				
1	1	3	1·262	0·701	0·260	0·041	1·002	0·260	20·60	79·40
2	1	4	1·723	1·285	0·108	0·166	1·559	0·164	9·52	90·48
3	1	7	1·360	0·613	0·116	0·079	0·808	0·552	40·59	59·41
4	1	7	1·778	1·010	0·076	0·031	1·117	0·661	37·18	62·82
5	1	7	1·423	0·526	0·127	0·119	0·772	0·651	45·75	54·25
6	1	7	1·162	0·784	0·060	0·071	0·915	0·245	21·08	78·92
7	1	18	1·782	0·000	0·114	0·140	0·254	1·528	85·74	14·26

Here it is noticed that although the quantity of milk given per kilo was very much the same in each case, the quantities of fat in the various parts in the alimentary tract differ very materially. For whereas in Exp. 1, the animal had passed nearly half of the fat from the stomach into the intestines, the dog in Exp. 2 during four hours passed very much less. The difference in the various dogs is clearly

marked in experiments 3, 4, 5, and 6, all of which were treated in an exactly similar manner. We find that the quantity of fat absorbed from the alimentary tract varies very remarkably. In Exp. 1, during three hours, 20·60 p.c. of the entire fat given was absorbed, while in Exp. 2, in four hours, only 9·52 p.c. disappeared from the alimentary tract. In this case the small quantity absorbed must, apparently, arise from some idiosyncrasy of the animal, such as is called in popular language, a slow digestion. For it is hardly possible that the excess in the large intestine can be responsible for it.

In Exp. 3, 4, 5, and 6 the percentage of fat absorbed varied from 21·08 to 45·75 the total given, i.e. 40·59, 37·18, 45·75, 21·08.

In Exp. 7, during eighteen hours, 85·74 p.c. of the total fat was absorbed.

It is seen in the above table that the quantity of fat disappearing from the stomach varies not only according to the time, but likewise to a certain extent, according to the individuality of the animal, even when the animals are kept as nearly as possible under similar conditions.

Tappeiner, von Anrep, Ogata, Edkins and von Mering seem to show that the stomach plays a very small *rôle* in the absorption of any materials introduced into it, and Contejean[1] has recently shown that pieces of fat placed in the stomach of dogs with gastric fistulæ, hardly diminish in weight at all.

It may therefore be taken for granted that all the milk fat which disappeared from the stomach had not been absorbed from it, but had passed through the pylorus into the intestine, and from thence had been absorbed. It is as well therefore to state in a tabular form the rate of passage of fat from the stomach.

TABLE 4. *On the rate of passage of fat from the stomach into the intestines.*

No. of Exp.	Time of digestion. Hours	Total fat given	Fat remaining in Stomach		Fat passed into Intestine	
			Total	p. c.	Total	p. c.
1	3	9·872	5·488	55·59	4·384	44·41
2	4	12·505	9·321	74·54	3·184	25·46
3	7	10·799	4·866	45·06	5·933	54·94
4	7	22·806	12·970	56·87	9·836	43·13
5	7	9·471	3·503	36·99	5·968	63·01
6	7	12·027	8·116	67·48	3·911	32·52
7	18	15·148	0·000	0·000	15·148	100·00

[1] Contejean. "Sur la digestion gastrique de la graisse." *Arch. de Physiol.* VI. 125.

We see in the above experiments that the rate of passage of fat from the stomach is extremely different. In Exp. 1 only 55·59 p.c. of the total fat remains in the stomach after three hours' digestion, while in Exp. 2, 74·54 p.c. remains. In Exp. 3, 4, 5, and 8 the quantity of food remaining in the stomach varies from 36·99 to 67·48 p.c., being respectively 45·06, 56·87, 36·99, 67·48. Only in Exp. 7 did the entire quantity of fat given leave the stomach. These differences can only be explained, by supposing them due either to variations in the peristaltic motor power of the stomach, or to the action of the sphincter muscle in the pyloric opening varying in the different animals.

As from the foregoing, it seems that no fat is absorbed by the coats of the stomach, but only by the intestinal canal, the following shows how much of the fat that is actually passed out of the stomach through the pylorus into the bowels, has been absorbed.

TABLE 5. *On the rate of absorption of fat from the small and large intestines.*

No. of Exp.	Quantity of fat traversed pylorus in grams	Time during which took place. Hours	Fat remaining in				Fat absorbed	
			Small intestine		Large intestine			
			Total	p. c.	Total	p. c.	Total	p. c.
1	4·384	3	2·032	46·35	0·139	7·28	2·033	46·37
2	3·184	4	0·782	24·56	1·207	37·91	1·195	37·53
3	5·933	7	0·923	15·56	0·634	10·69	4·376	73·76
4	9·836	7	0·977	9·93	0·402	4·09	8·457	85·98
5	5·968	7	0·845	14·16	0·791	13·25	4·332	72·59
6	3·811	7	0·623	15·93	0·740	18·93	2·548	65·16
7	15·148	18	0·970	6·40	1·191	7·86	12·987	85·74

We see in Exp. 1 and 2, which lasted respectively three and four hours, the percentage of fat absorbed by the small and large intestines was 46·37 and 37·53, not nearly so great a difference as we previously showed when regarding the fat in the entire alimentary canal. In Exp. 3, 4, 5, and 6, all of which lasted seven hours, the percentage of fat absorbed varied from 65·16 to 85·98, being respectively 73·76, 85·98, 72·59, 65·16. While in Exp. 7, lasting eighteen hours, 85·74 p.c. of the fat was absorbed, resembling very closely that which had been found in Exp. 4.

From these results it may be concluded that the rate of fat absorption from the intestines in dogs varies with the time allowed for digestion, and it does not vary so much in individual dogs, as the rate

of the passage of fat from the stomach into the intestines does. Further, that the maximum rate of absorption of fat occurs about seven hours after the taking of food, and this is not exceeded when it is allowed to digest longer, although the supply be kept up by the passage of fresh fat from the stomach until it is completely emptied.

In all the above cases the absorption of fat may be somewhat less than the normal, as we know that prolonged fasting diminishes the power of forming the various normal digestive secretions. For this very reason the results here recorded are all the more valuable for comparison with those now to be described on the absorption of fat after the removal of the pancreas.

The Absorption of Milk Fat after the Total Extirpation of the Pancreas.

Having in the preceding part shown the results of the absorption of milk fat in dogs in which the pancreas has not been extirpated, before we do the same thing with those in which the gland has been removed, it will be as well to give a short account of what has up to the present been found out, regarding the absorption of fat in cases where the pancreatic juice is prevented from reaching the intestines.

S. Collin[1] stated that contrary to the view of Cl. Bernard the absorption of fat remained undisturbed when the pancreatic juice was allowed to escape from a fistula. It had been clinically observed by Bright[2] as early as the year 1832, that in cases of disease of the pancreas the fat was very incompletely absorbed, and appeared in large quantities in the stools.

Cash[3] cut the chief duct of the pancreas, and by means of injecting Berlin blue was able to find the second smaller duct, which was also cut and ligatured. Four days later when the dog had recovered from the operation, he fed it on neutral fat. The lymphatics were found at the autopsy to be filled with lymph, so that these dogs had evidently been capable of absorbing fat.

In 1889 von Mering and Minkowski[4] in their now classic work, in which they showed that the total extirpation of the pancreas invariably

[1] S. Collin. "De la digestion et de l'absorption des matières grasses etc." *Bulletin de l'académie de Méd.* 1856.

[2] Bright. *Med. Chirurg. Trans.* 1832.

[3] Cash. *loc. cit.*

[4] von Mering and Minkowski. *Arch. f. exp. Path. u. Pharm.* XXVI. 371, 1889, and other papers.

rendered dogs diabetic, noticed that these animals passed always large quantities of fat in their fæces.

M. Abelmann[1] showed that after complete removal of the pancreas, fat in the form of olive oil, butter, etc. appeared again entirely in the stools, while fat in the form of milk given by mouth was absorbed on an average about 49·8 p.c. In the cases he quotes the difference varies within wide limits, some only absorbing 28 p.c., others 53 p.c. Minkowski[2], in a paper in which he discusses the subject, comes to the conclusion that Abelmann's experiments clearly support C. Bernard's view that the pancreatic juice is absolutely necessary for the absorption of fat (i.e. butter, olive oil, etc.) from the intestines, and that no other digestive secretion can take its place.

That the action of the pancreatic juice cannot be put down to the want of splitting up of neutral fat, has been already pointed out. Abelmann showed that the ether extract of his dogs' fæces contained 80 p.c. as free fat acids, and only a small portion as soaps. Hédon and Ville[3] showed that when bile was prevented from entering the intestine the fæces contained 41 p.c. of soap, 57 p.c. fat acid and 2 p.c. neutral fat. If then the greater part of the pancreas was removed, the tail being left to prevent the glycosuria, they then contained 45 p.c. as fat acid, 55 p.c. neutral fat, but no soap, milk being used as the diet.

These conflicting results led me to the investigation which I am now about to describe, for it is difficult to see if fat can be split up without the pancreatic juice, why it should not also be absorbed.

In some experiments I performed in Turin on the absorption of fat after total extirpation of the pancreas, I obtained results which showed an absorption of fat varying from 10 p.c. to 40 p.c. of the fat given, when the method of feeding and analysing the fæces was employed. It is to be remembered that a dog after the total extirpation of the pancreas suffers from so severe form of diabetes, that it not only rapidly loses strength and weight, but that its entire metabolism must be very markedly disturbed. Again, in these dogs the fæces always have a most offensive odour, and as bacteria are known to be able to split up neutral fat, the various quantities of these present in the alimentary canal might be the cause of the differences found.

I therefore in the experiments about to be described adopted the method already mentioned of keeping the dog fasting four days, and

[1] M. Abelmann. *Inaug. Dissert.* Dorpat, 1890.

[2] Minkowski. "Zur Lehre von der Fettesabsorption," *Berl. klin. Woch.* 1890, p. 333.

[3] Hédon and Ville. *Comp. Ren. Soc. Biol.* 1892, p. 308.

then, after feeding with the milk food, killing at a certain number of hours. In studying the absorption of milk fat after the removal of the pancreas, it will be as well to tabulate them in the same manner as was done in the normal dogs already described.

TABLE 6. *Absorption of milk fat after the total extirpation of the pancreas.*

No. of Exp.	Weight. Kilos	Time of digestion. Hours	Total fat given	Fat remaining in			Total fat found	Remarks. + or −
				Stomach	Small intestine	Large intestine		
*1	9·637	4	20·037	9·947	9·773	0·409	20·129	+ 0·092
2	6·188	4	7·602	7·406	1·456	0·444	9·306	+ 1·704
*3	4·365	5	6·638	4·397	2·497	0·603	7·497	+ 0·859
*4	8·276	6	13·652	8·029	4·081	1·865	13·975	+ 0·323
5	6·975	6	8·496	7·624	0·822	0·251	8·697	+ 0·201
6	5·400	7	7·191	6·554	1·077	0·644	2·275	+ 1·084
7	6·750	7	12·027	9·358	0·464	1·672	11·494	− 0·533

In those marked thus * the pylorus was not tied until after removal from the body.

As is seen in the above table the results obtained were very remarkable. For not only is the total amount of fat given again found in the alimentary tract, but even in all but one case an excess over what was given (Exp. 7) and that was when the animal had diarrhœa, although as much as possible of the fæces were collected from the floor, some were probably lost which would account for the loss here found.

The quantity of fat in the small intestine of Exp. 1, 3, and 4 is possibly too large, for a part of the fat may have really belonged to the stomach, as the stomach and intestines were removed from the animal before the pylorus was ligatured.

On examining the table in detail it is found that the quantity of fat in the stomach is very much higher than in the normal dogs.

The quantity of fat in the small intestines is also greater than in the normal animals, when the three cases just commented upon are excepted.

In the same manner as was previously done, in the following table the amount of milk fat is expressed per kilo of animal weight.

TABLE 7. *Amount of milk fat calculated per kilo of animal weight.*

No. of Exp.	Time of digestion. Hours	Fat given	Fat found in			Total fat found	Remarks. + or −
			Stomach	Small intestine	Large intestine		
*1	4	2·079	1·032	1·014	0·042	2·089	+ 0·010
2	4	1·229	1·197	0·235	0·072	1·504	+ 0·275
*3	5	1·521	1·007	0·572	0·138	1·718	+ 0·197
*4	6	1·650	0·970	0·493	0·225	1·689	+ 0·039
5	6	1·218	1·093	0·118	0·036	1·247	+ 0·029
6	7	1·332	1·214	0·119	0·199	1·532	+ 0·200
7	7	1·782	1·386	0·069	0·248	1·703	− 0·079

In comparing this table with the corresponding one on normal dogs, it is seen the quantity of fat given per kilo is very similar, and the quantity of fat in the stomach is very much larger than that found in the normal dogs.

In table 3, it is seen that in the small intestines after 3 and 4 hours' digestion only 0·260 and 1·108 grams are present while in the pancreatic dogs' table 7, there is 1·014, 0·235 and 0·572 grams, in Exp. 1, 2, and 3.

On the other hand this average is still higher in the case of dogs which have had longer to digest—in table 3, the 4 dogs which digested 7 hours had an average of 0·095 grams in their small intestines (0·116, 0·075, 0·127, 0·060) while in table 7, the two dogs which digested 6 and 7 hours had an average of 0·158 (0·118, 0·199), as Exp. 4 must be omitted for the reason already given, and Exp. 7 as the dog had diarrhœa.

The same does not hold good as regards the larger intestine; in the normal the average is 0·113 grams during 3 and 4 hours (0·041, 0·166) while in Exp. 1, 2, and 3 the average is 0·084 grams (0·042, 0·072, 0·138). In the normal dogs during 7 hours the average is 0·903 grams (0·808, 1·117, 0·772, 0·915) while the pancreatic dogs are 0·157 grams (0·225, 0·036, 0 119, 0·248).

As it is seen from the above table that the fat apparently passes very slowly from the stomach into the intestines in dogs after removal of the pancreas, it may be well to present this in a tabular form as has been done in the case of normal dogs.

TABLE 8. *The rate of passage of fat from the stomach into the intestine after extirpation of the pancreas.*

No. of Exp.	Time of digestion. Hours	Total fat given	Fat remaining in Stomach		Fat passed into Intestines	
			Total	p. c.	Total	p. c.
2	4	7·602	7·406	97·42	0·196	2·58
5	6	8·496	7·624	89·74	0·872	10·26
6	7	7·191	6·554	91·14	0·637	8·86
7	7	12·027	9·358	77·81	2·669	22·19

From the above table Exp. 1, 3, and 4 have been omitted for the reasons above alluded to.

The results are here found to be no less remarkable than they were in the case of absorption of fat just described. In the normal dog in four hours even in the case when there appeared to be a diminished motility, the stomach had passed on into the intestines no less than 25·45 p.c. of the fat given, while in the above Exp. 2, only 2·58 p.c. had traversed the pylorus.

In seven hours in normal dogs from 32 to 63 p.c. of the fat had left the stomach, while in Exp. 6 and 7 in the above table only 8·86 and 22·19 p.c. had passed into the intestine. In Exp. 7 the larger quantity which had left the stomach was probably due to a hurrying of the passage of fat along the alimentary canal, owing to the diarrhœa.

It can be therefore concluded that after extirpation of the pancreas there is a marked delay in the expulsion of fat from the stomach. This no doubt is due to the diminished peristalsis, the result of the general weakness occurring on account of the diabetes.

It is as well to state that in all the dogs in which the pancreas had been removed, there was more or less glycosuria in spite of their being kept without food. The quantity of sugar passed varied in the different dogs from 1 to 7 p.c. Polyuria was in some cases present, but never to any very marked extent. In most of the urines examined acetone was found, and in some of the cases aceto-acetic acid.

They all suffered from a marked loss of flesh, especially so when compared with the normal dogs, for in only one case did a normal dog lose one kilo of its weight during the four days, while those in which the pancreas had been removed lost, during the same period of time, from $1\frac{1}{2}$ to $3\frac{1}{2}$ kilos.

The next question is, how can be explained this increase in the total

quantity of fat found in the intestines after the removal of the pancreas? These results seemed to be cleared up by the researches of Hermann[1], Ehrenthal[2], Berenstein[3], and Fr. Voit[4]. These observers isolated a loop of intestine, either by sewing the two ends together so as to form a ring, or by stitching up the two ends. The intestine was then joined below the isolated part and the dogs allowed to live. The isolated part in about three weeks became filled with a semi-solid material. Hermann considered this material to arise from the intestinal secretion, which in the interval had, by the absorption of its fluid parts, become converted into a pappy consistency. Ehrenthal regarded it as principally broken down epithelium derived from the intestinal mucous membrane, on account of his finding in the inner surface a white gluey like substance, which microscopically appeared to consist of more or less degenerated epithelial cells. In Hermann's dogs, which lived somewhat longer, no outer zone was found and the mass itself contained very few epithelial cells. Berenstein, who disinfected the intestinal loop so that micro-organisms should not be the cause of desquamation, found the mass was not merely composed of epithelial cells, but principally concentrated intestinal secretion. Fr. Voit showed that the mass besides containing nitrogen and salts when dried, in some cases contained as much as 36 p.c. of fat. I have found that the same mass accumulates in the large intestine when it is treated in a similar manner.

It would appear from the foregoing that the surplus fat found in those dogs in which the pancreas has been removed, is due to this intestinal secretion or excretion. Whether or no any of the fat was absorbed from the intestines of my dogs, I am not prepared to say. For at the autopsy although the intestinal lymphatics were not filled with chyle as in normal dogs, they always appeared more distinct than one usually sees in a fasting dog. This was more markedly the case in the lymphatics of the large intestine.

The fact that Abelmann found that some absorption of milk fat occurred in his dogs may be accounted for by the bacteria of the intestine having aided in the absorption. In my cases the repeated washing out of the lower bowel with warm water coupled with the animals having fasted, might have reduced the micro-organisms to a very small quantity.

[1] L. Hermann. *Pflüger's Arch.* XLVI. 93. 1890.
[2] W. Ehrenthal. *Pflüger's Arch.* XLVIII. 74. 1891.
[3] M. Berenstein. *Pflüger's Arch.* LIII. 52. 1892.
[4] Fr. Voit. *Zeit. f. Biol.* XXIX. 325. 1892.

It would appear that the presence of large quantities of fat in the stools would point very strongly to an absence of pancreatic secretion reaching the alimentary tract.

Conclusions:—1. Normally a dog absorbs from 9 to 21 p.c. of the total fat given in 3 to 4 hours; from 21 to 46 p.c. in 7 hours and 86 p.c. in 18 hours.

2. In a normal dog the passage of fat from the stomach varies with the individual as well as with the time allowed for digestion. In 3 to 4 hours 25 to 44 p.c. of the fat given has left it; in 7 hours 33 to 63 p.c.; while in 18 hours the total has entered the intestines.

3. In normal dogs, of the fat that has actually entered the intestines and therefore is under favourable circumstances for absorption 37 to 76 p.c. is absorbed in 3 to 4 hours, 65 to 86 p.c. in 7 hours, while 86 p.c. is absorbed in 18 hours.

4. In dogs which have had their pancreas removed the quantity of fat given is not only again recovered but a surplus is found, which is probably derived from the intestinal secretion or excretion.

5. The power of passage of fat from the stomach is very much delayed by the extirpation of the pancreas. Such dogs only passing in 4 to 6 hours from 3 to 10 p.c. of the fat given into the intestines, while in 7 hours only 9 to 22 p.c. has traversed the pylorus.

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REMARKS ON THE CHEMICAL PATHOLOGY, SYMPTOMS, AND TREATMENT OF URIC ACID GRAVEL.

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Experimental medicine has during the last two decades been especially turned towards bacteriology, and consequently the important branch of pathology embraced in the word "metabolism" has received but scant attention. In spite of this, as regards the question of uric acid formation so much has been done in this direction that it may be said our views are entirely different from what they were a quarter of a century ago, and we are now able to treat patients suffering from uric acid disease on new scientific instead of old empirical principles.

As it would take up too much time to discuss the entire uric acid diathesis, I will merely call attention to that form known under the name of uric acid sand or gravel, and leave the question of its concretions with gout entirely out of the question.

Our first step in an inquiry into the causation of uric acid gravel is as regards the formation of uric acid in the organism. Until quite recently uric acid was regarded as one of the normal products resulting from the breaking down of proteids in the processes of metabolism. Sir William Roberts regarded it in man as a vestigial feature of some ancestral form. Chemists had succeeded by a process of oxidation and hydration in converting uric acid in the test tube through the transitional stages of alloxan, parabamic acid, oxaluric acid, and oxalic acid into the final products of urea and carbonic acid. Physiologists considered that proteids passed

through the stage of uric acid in the animal body before being converted into urea by oxidation. If, then, uric acid is under normal circumstances oxidised in the animal body into urea and carbonic acid, one might expect that in diseases in which oxidation is hindered there would be an increase in the uric acid eliminated into the urine. Contrary to this expectation, Senator, as early as 1868, failed to find any increase in the uric acid in the urine when the respiratory processes were artificially interfered with, and Naunyn and Reiss equally obtained negative results when tissue oxidation was retarded by venesection. Further, pathology shows us that in simple anæmia there is no increased elimination of uric acid.

Bunge explains the failure of the oxidation theory by calling attention to the fact that in birds in whom respiration is most active the bulk of the nitrogen is eliminated as uric acid. While Frerichs, Wöhler, Zabelin, and others had previously shown that when uric acid was given, either by the mouth or intravenously, it appeared in the urine as urea, and no increase of uric acid could be recognised. Haig has lately pointed out that this is probably due to precipitation of uric acid in the organs, and if it is given while the blood is kept alkaline there is really an increased elimination of uric acid in the urine. It thus follows that, experimentally, we have no evidence that uric acid is converted into urea in the organism.

The researches of Horbaczewski, Kossel, etc., have led to the view that uric acid is not derived from the metabolism of the general proteids which yield urea, but from nuclein derived from the nucleo-albumin of the cells. Horbaczewski showed that when splenic pulp is mixed with blood and kept for some time at the temperature of the body it yields xanthin bases; and that when the same process is carried out in the presence of an abundant supply of oxygen instead of xanthin bases uric acid is formed.

The constituent of the spleen which yielded these xanthin bases was found to be nuclein. Other observers, in addition, found that all the tissues of the body that contain nuclein are in like manner capable of yielding uric acid.

Horbaczewski further showed that feeding animals with nuclein, or injecting it subcutaneously, causes an increase in the elimination of uric acid, not only in animals, but also

in man. This last statement has been contradicted by Stadthagen in the case of dogs, in whose urine he says he found, if anything, the amount of uric acid decreased, and, on the other hand, the urea markedly increased.

These contradictory statements have likewise been made, as already stated, as regards the effects of feeding with uric acid, and we must leave them for the present for further investigation.

We can now turn to observations made on man to see if we find this nuclein view of uric acid formation supported.

Marès examined the urine as to the quantity of uric acid excreted from time to time, and found that, after a meal, it rose rapidly, so that in two to five hours it had reached double or even three times what it was during fasting; it then slowly fell for the first thirteen hours after food, and then remained constant until fresh food was taken. He found the rise was greatest after animal less after vegetable diet. Urea, on the other hand, does not begin to be increased in quantity until some time after food, and only reaches its maximum nine or more hours after the meal, and then still more gradually falls. It is known that after a large meal, especially of animal food, a great increase of leucocytes takes place in the blood, and at the time that they are being destroyed and their nuclein liberated it appears that there is this increase in the amount of uric acid eliminated in the urine.

As early as in the year 1868 Bartels showed that in leucocythæmia four times the normal amount of uric acid was eliminated with the urine in twenty-four hours. Schultzen, Ebstein, and others have confirmed the statement that the quantity of uric acid is always markedly increased in this disease.

Fleischer and Penzoldt, on comparing the quantity of uric acid passed by a leucocythæmic patient with that of a healthy patient on the same diet, found that while the first was more than double the amount of uric acid eliminated by the healthy man, the quantity of urea excreted was the same in both cases. This fact of the urea remaining the same shows that the nitrogenous matter taken as proteids in the food was equally eliminated in both cases, while the excess of leucocytes in the blood of the one caused an excessive breaking down of them in this case and a proportionate excess of uric acid.

Lately von Jaksch found that in pneumonia, when there is an increase of leucocytes in the blood, there is at the same time an increase in the uric acid present.

Moreover, it has been for some time past known that phosphorus and pilocarpin induce a leucocytosis which is also accompanied with an increase of uric acid in the urine. The same thing again holds good for alcohol; both Chittenden and Cameron found that both in animals and man the taking of alcohol caused an increase in the quantity of uric acid in the urine.

If we have these pathological supports to the nuclein view of the uric acid formation, we find we have an equally good physiological one in the case of children. In early life the number of leucocytes to red blood corpuscles is much greater than in adult life, as shown in the following table:

Table showing Number of Red Blood Corpuscles to Leucocytes at various Ages in Males.

Author.	Age.	White.	Red.	Proportion of White to Red Corpuscles 1=
Dupérié	2 months	8,200	4,433,000	541
,, ...	2 years	3,900	4,805,000	1,232
Bouchut and Dubrisay...	2½ to 15	6,704	4,269,000	648
Rieder	11 to 15	9,800	—	—
Dupérié	18	3,900	5,704,000	1,463
,, ...	26	6,700	6,138,000	916
Bouchut and Dubrisay...	20 to 30	6,113	4,192,687	700
,, ,, ,, ...	30 to 58	—	4,080,113	616
Dupérié	69	4,700	4,898,000	1,042
,, ...	78	5,400	4,712,000	873

The quantity of uric acid eliminated daily is also relatively larger than in later life, so that clinical experience supports the view that uric acid is a derivative of nuclein.

The Seat of Uric Acid Formation.

As regards the organs or organ in which uric acid is formed, we are still very much in the dark. Schröder, who experimented by either extirpating the kidneys or shutting them off from the circulation in hens, found that the uric acid accumulated in all the organs of the body; and that in snakes which survived the operation for some days, this increase in the quantity of uric acid in the organs was still more marked. It thus appears that both in the case of birds and snakes uric acid cannot be said to be formed only in the kidneys. Clinically, in kidney disease, in which elimination of urine

has been hindered, an increase in the uric acid of the body has been found to follow, so that in all probability the same holds good for man.

Meissner in 1868 pointed out that normally the quantity of uric acid is always higher in the liver than in the blood of birds.

Minkowski, who succeeded in keeping geese alive from six to twenty hours after extirpation of the liver, found that, while in the normal goose from 60 to 70 per cent. of the total nitrogen is eliminated as uric acid, after the liver is extirpated only from 3 to 6 per cent. is passed as uric acid. On the other hand, the ammonia increases after the hepatic extirpation, so that 50 to 60 per cent. of the total nitrogen is in this form, while in healthy geese only 9 to 18 per cent. of the nitrogen appears as ammonia.

From the results obtained in the above-alluded-to experiments, one is led to look upon the liver as the principal seat of uric acid formation. Indeed they might have been regarded as conclusive had not experiments made conjointly by Hahn, Massen, Nencki, and Pawlow led to opposite conclusions. They shut the livers of dogs almost completely off from the general circulation by diverting the portal circulation into the inferior vena cava, and found that, although the dogs passed less urea (the nitrogen being nearly all eliminated in the form of carbamate of ammonia), the uric acid voided was considerably increased.

From this summary of the recent experimental work on the genesis of uric acid, it appears that, although we have made considerable progress in discovering what are the precursors of uric acid in metabolism, the actual seat of its formation is a point still unrevealed to us.

The Cause of Uric Acid Precipitation in Urine.

It has been shown by Sir William Roberts that the uric acid always exists in the urine in the form of quadriurates. According to him, the first step in the precipitation of uric acid is the breaking up of the quadriurates by the action of water into a biurate, and the setting free of a quantity of uric acid, which from being but slightly soluble is precipitated, while the more soluble biurate remains in solution. The next step is that the biurate is acted upon by the monometallic phosphate and thereby converted into the quadri-

urate, and the phosphate itself being converted into dimettalic phosphate—2 $MH\bar{u}+MH_2PO_4=H_2\bar{u}$, $MH\bar{u}+M_2HPO_4$. This process is continued either until all the urates are precipitated as free uric acid or alkaline fermentation sets in.

If this view be correct, it follows that in urines which do not precipitate uric acid there must be a something which hinders this breaking up of the quadriurates by the action of the water. This something appears to be the sulphates, chlorides, and phosphates, as well as the colouring matter of the urine; the potassium salts appear to act more powerfully in this way than the sodium or ammonium ones, while a fixed alkali entirely prevents the change taking place.

The acidity of healthy urine is now known to be due not to the presence of free acids, but to the acid salts such as acid phosphate of soda (NaH_2PO_4). This is derived from the blood, and it was supposed the basic sodic phosphate (Na_2HPO_4) was converted into the acid by the uric acid, hippuric acid, sulphuric acid, etc., taking themselves part of the soda, or that acid salts more readily diffused through the kidney.

Neither of these explanations was very satisfactory, and Liebermann has now shown that the kidney substance contains an acid-reacting substance (lecithin-albumin) which is capable of converting an alkaline reacting salt (such as Na_2HPO_4) into an acid one, and that even blood serum, or defibrinated blood, when filtered through a layer of lecithin-albumin, is converted into an acid filtrate. An alkaline solution of Na_2HPO_4, when artificially circulated through a freshly extirpated dog's kidney, yields an acid urine. In the normal formation of urine the bases which combined with the acid lecithin-albumin are in their turn broken down by the carbonic acid formed in the tissues, so as again to set free the acid lecithin-albumin for renewed action. If this view is correct, under ordinary circumstances, a sufficient quantity of alkaline (Na_3HPO_4) salts being present in the blood, the renal cells do not break up the soluble urates in their passage into the urine. When, however, this equilibrium is upset by a diminution of the alkaline salts, the soluble urates being in normal quantity, the renal cells will set free uric acid, which will be precipitated in the urinary tubules; or, if the urates

are in excess, the alkaline salts may fail to be in sufficient quantity to keep the urates in a soluble form.

Liebermann found if a saturated solution of uric acid in Na_2HPO_4 be divided into two parts, and one of them diluted with water and the other with Na_2HPO_4, when they are passed over lecithin-albumin, the latter contains the most uric acid, from less of it having been retained—that is, precipitated. An excess of lecithin-albumin in the kidney, it is thus seen, would lead to an acid urine being excreted; and it looks as if the alkaline urine of herbivora is due to the amount of lecithin-albumin in the kidneys not being sufficient to break up the alkaline salts of their diet.

The Cause of Uric Acid Gravel.

Having discussed the chemistry and physiology of uric acid, it behoves me now to turn to the pathology of the state we know as uric acid gravel.

Under the head of uric acid gravel we place that diseased condition in which uric acid is precipitated in the urine either in the tubules of the kidney, urinary tract, or in the urine immediately after being passed. We have already seen that uric acid under normal conditions is kept in solution in the urine by certain means, and, further, the quantity found in the animal body depends upon certain definite circumstances. The appearance of a precipitate of uric acid can arise from two causes:

First, an excessive formation of uric acid whereby the solvent power of the urine is insufficient to keep the increased quantity in solution.

Secondly, a diminution in the quantity of the natural solvents for uric acid in the urine, which leads to its precipitation, although the total quantity may be normal or even less than the normal standard.

As regards the first cause we know that hereditary predisposition plays an equally important part in uric acid gravel deposits as it does in gout. The hereditary cases in which there is a total daily increase of uric acid may be put down, according to our present knowledge of the matter, to some more or less marked form of leucocytosis. In children, in whom uric acid gravel is common, new cells are both rapidly built up and rapidly broken down, and in them the leucocytes of the blood are in a greater proportion than in adults, as has been previously stated.

In the next place, the kind of diet is supposed to have an important influence on uric acid gravel, animal proteids seemingly increasing it more than vegetable. As regards the daily quantity of uric acid passed, A. Herman found on a vegetable diet 0.478 grammes, on a mixed diet from 0.636 to 0.674 grammes, and on an animal diet as much as 0.981 grammes. Marès obtained equally strong results favouring the supposition that animal proteids lead to a larger formation of uric acid than vegetable proteids do. Alcohol, also as already stated, increases the quantity of uric acid formed. The taking of large quantities of water was found by Schöndorff and others to have no influence on the quantity of uric acid eliminated. The former found the following tabulated results in an experiment extending over a month:

Diet.	Uric Acid per Diem.	Total Nitrogen per Diem.
	Grammes.	Grammes.
Ordinary diet	1.184	18.5
,, ,, + 2,000 c.cm. H_2O... ...	0.931	20.4
,, ,, + 4,000 c.cm. H_2O... ...	1.016	20.6
,, ,, + 1,000 c.cm. H_2O... ...	1.143	23.8

Muscular exercise has also an effect on the daily amount of uric acid excreted. Levison found—that in his case being subject to uric acid gravel—horse riding increased the uric acid output in one experiment from 0.6 grammes to 0.981 and 0.955 grammes, and in another to 1.089 grammes. Excessive muscular exercise tends to a leucocytosis, so would explain the increased uric acid elimination. The exercise may not be excessive in the ordinary sense of the word, but horse riding in one not accustomed to it would be classed under the same head.

If we turn to the second cause of uric acid gravel, we find heredity here also probably plays an important part. It has been by many observers noticed that urines that tend to deposit uric acid are often very pale. I have frequently found these pale urines depositing uric acid, although the total quantity is not increased, are to be especially met with in people suffering from the condition we now recognise under the head of neurasthenia, and this is, as you all know, often hereditary.

Diet alone also plays an important part in this form of uric acid precipitate when no excess of uric acid occurs. The mere taking of food poor in salines increases the tendency to gravel, and that even when the daily quantity of uric acid excreted is very small, as, for example, when an almost starving amount of food is being taken. Sir W. Roberts pointed out that uric acid concretions are common among Hindus, who live almost exclusively on rice, a food poor in salines. Hutchinson showed that uric acid gravel is rare among sailors, who eat salt meat and consequently take in a superabundance of salines, while naval officers, who live much the same life but take fresh meat, are by no means immune. Muscular exercise, when carried to excess, has also a tendency to increase the acidity of the urine, and hence the deposit of uric acid by this means.

Symptoms and Diagnosis of Uric Acid Gravel.

The principal factor in this condition is naturally the presence of free uric acid crystals in the urine either before or immediately after being passed. The recognition of these crystals is often somewhat difficult from a specimen of the day's urine being examined. It is as well always to remember the urine is most acid after a long fast, such as takes place during the night, and therefore one ought to examine an early-morning specimen.

In cases where the precipitation of uric acid takes place in the urinary tubules it irritates their epithelial lining and hence causes the formation of hyaline casts. In some cases the irritation is to such an extent as to cause albumin or even blood to appear in the urine.

Ultymann and Leube say that the so-called periodical albuminuria is often due to uric acid sand.

I think all observers who have employed the centrifuge in the separation of the urinary deposit are agreed that hyaline casts are a common accompaniment of uric acid crystals. I have frequently met with them as well as occasionally cases in which uric acid crystals were embedded in granular casts. These uric acid casts are best found in urine passed in the early morning and centrifuged while fresh. *Débris* of epithelial cells are nearly always found when the centrifuge is employed, and in some cases the deposit reveals the existence of a pyelitis.

In cases belonging to the second group, in which the uric acid is not in excess, the urine is nearly always very acid, and generally much paler than normal urine. In fact it is what one would call a very watery urine.

A good rough test to recognise a tendency to uric acid deposit, even when no precipitate occurs, is to pour very slowly into a test tube nitric acid so that a layer forms. The urine thus treated, if it shows a cloudy ring above the junction of the two liquids before it has stood five minutes has a tendency to deposit uric acid; if between five and ten minutes it is normal; while when it takes longer than ten minutes either the total quantity of uric acid is below normal or it contains more than the usual amount of solvents. This uric acid ring lies above the ring formed when albumin is present, so in such cases one gets two rings.

The symptoms of uric acid gravel vary from being most marked and pointing definitely to the urinary tract to very doubtful ones. I only intend here to mention those symptoms which arise from the presence of uric acid crystals in the urine, and not those due to its excess or otherwise in the blood. In a typical attack lumbago-like pain in the kidney region extends down in front, along the course of the ureters, into the groin, accompanied by pain in and retraction of the testicles (in women pain in the ovary). This pain is accompanied by a frequent desire to pass water. There is inability to stretch down the legs, and the necessity of keeping them in a flexed position, with the feet towards the scrotum, and the knees thrown outwards. Great relief is here obtained by putting a pillow under the knee and bending the leg over it.

When gravel is impacted in a ureter pain may be intense, and the tenderness on pressure apt to be mistaken for peritonitis. The tenderness does not radiate so much over the abdomen. Vomiting frequently occurs, and when pain is very acute one may even have delirium. These symptoms are so closely allied to those of renal calculus, and as I am now only dealing with the smaller forms of uric acid gravel, I will now turn to the more indefinite ones.

In slight cases the lumbar pain may be expressed by the patient as merely a "tender feeling" over the loins, or it may be a heavy, dull pain which ceases on going to bed, to return on rising in the morning. This pain may diminish somewhat

during the day, but never entirely goes away. It is aggravated each time the patient assumes a new position, and is often on that account mistaken for a lumbago.

The pain may radiate from the back in various directions, either towards the stomach or the shoulders, and even occasionally, according to Levison, down the arms. I oftener find it in the legs, and have had it described to me as a sciatica, which it can as a rule be distinguished from by the course it takes being more towards the front than the back of the thigh.

Various forms of neuralgia—as, for example, migraine, angina, asthma, etc.—are said by Da Costa to accompany uric acid gravel. Irregular action of the heart is a frequent accompaniment of the passing of gravel. Levison says constipation is a common occurrence; but this as a rule is, I think, due to some other cause than mere gravel. Frequent micturition is an accompaniment of even the mildest forms of uric acid gravel, and can be explained by reflex irritation.

In children, in mild cases the presence of uric acid sand is often overlooked on account of the child never complaining of any actual pain. Such cases only are recognised by examination of the urine on account of the child suffering from a frequent desire to micturate, which may be attended with sudden fruitless desires to go to stool, and a general restless nature. An ordinary examination of the urine often fails to discover anything abnormal about it. If, however, a fresh specimen of the morning urine is examined by means of the centrifuge, crystals are recognised and the case easily diagnosed.

In more severe cases, as pointed out by Sutherland, Goodhart, etc., the symptoms are more marked. Pain commonly occurs, which is as a rule not referred to the kidneys but to the umbilical or iliac region. The children are restless and active, sleep badly, and often talk while asleep. Besides the presence of uric acid crystals in the urine, albumin is often intermittently present, and tube casts, when properly looked for, are usually found. Frequent desire to micturate and the desire to go to stool also accompany these cases.

Treatment.

The treatment of uric acid gravel takes two directions, according as we desire to increase the solubility or decrease the amount of uric acid formed. It is well to remember that

in the majority of cases uric acid deposits are due to an increased tendency to precipitation, and not to excessive formation of uric acid.

In cases due to an increased tendency to precipitation, we have to give drugs which help to hold uric acid in solution. In spite of the recent outcry against piperazin, I must say I have found it of great service, particularly in all cases in which gravel has been due to diminished solvents and not excessive formation of uric acid. In fact it appears to me to have no action whatsoever on the quantity of uric acid daily formed in the organism, but merely on its solubility. On this account I always give it in such cases in combination with alkalies either in the shape of alkaline waters, or potash bicarbonate combined with iodides. It is as well to remember that as the urine is naturally most acid at night and early morning, and therefore most likely to deposit uric acid, we can get over this by following Sir William Roberts's advice, and give the alkalines at bedtime. The diet in these cases is not of so much importance except in favour of salines and vegetables.

In cases, again, when the uric acid deposit is due to excessive formation, a carbohydrate diet is the most useful. Starch, sugar, and vegetables should, therefore, be the staple diet, and meat and fish only in small amounts. The old idea that sugar causes an increase of uric acid has no foundation, as I found in a series of experiments performed on myself when I took as much as a quarter or even a pound of sugar a day without causing any noticeable increase in the uric acid passed. Alcohol, on the other hand, should be prohibited, as it causes an increase in the quantity of uric acid voided.

Quinine and arsenic decrease the quantity of uric acid because they diminish the quantity of leucocytes, and therefore in cases where gravel is due to an excessive formation of uric acid they are most valuable. While moderate muscular exercise is of service, excessive exercise is, on the other hand, harmful.

In cases of excessive formation, although alkalies are of some assistance, they, like piperazin, are only of secondary importance by increasing the solubility of the uric acid formed.

The subject of treatment could well be gone into much more fully, but I think I have said sufficient to indicate the general principles on which it should be conducted.

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THE FUNGUS-FOOT DISEASE OF INDIA.

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and

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Since our last paper read before the Royal Society[1] on the "Fungus-foot Disease of India," our work has been chiefly directed towards cultivating the organisms found in both the varieties of the disease, namely, the black and white, and we have to thank Brigade-Surgeon-Lieutenant-Colonel Keith, of Hyderabad (Sind), and Surgeon-Major Hatch, of Bombay, for placing fresh material at our disposal.

Numerous glycerine-sugar-agar tubes were inoculated by Dr. Keith and his assistant Dr. Bocarro, and sent over to England; while in Bombay one of us had the opportunity of making inoculations on similar tubes from a case of the white variety which was in the J. J. Hospital under Dr. Hatch. The great difficulty experienced both here and in Bombay was to get the cultures free from putrefactive and pyogenic micro-organisms. In March last Dr. Boyce succeeded in getting a tube with white particles which showed hardly any contamination, and the result has been the culti-

[1] *Proceedings of the Royal Society*, 1893. *Transactions of the Royal Society*, April, 1894.

vation of a streptothrix.[1] Dr. Vincent, of the Pasteur Institute, Paris, has been working at the same subject, and he has kindly placed at our disposal cultivations of a similar streptothrix from a case of the white variety which he came across in Algiers.

In the present communication we give an account of the life-history of the organism, and compare it with similar organisms, especially actinomyces. This organism grows very slowly on most of the nutrient media we have tried. In gelatine and broth it does not seem to grow at all, but cultures taken from these media begin to grow when transferred either to potatoe or glycerine-sugar-agar. On these media the growth does not appear to make any progress for about a week, but after that the margin round the inoculated area shows slight projections, which thicken gradually, and give to the growth a radiate appearance. Minute colonies are formed round the central growth, and these show a cross-like depression, which becomes more marked as they increase in size. The growth is firmly adherent to the nutrient medium at the margins, while the central part is loosely attached. Its colour is dull white or slightly pinkish. When manipulated with a platinum needle it appears like brittle membrane, and crumbles to pieces on trying to tease out a particle. The mode of growth is almost identical on agar and potato. It grows best in oxygen at a temperature of 37° C. on glycerine-sugar-agar, or potato, rendered alkaline by being boiled in sterile broth, stab inoculations only grow at the surface. In an atmosphere of hydrogen the growth is excessively slow. In this respect it differs from actinomyces, which grows easily in an atmosphere of hydrogen. Coverglass preparations take up the aniline stains very easily. The best results are obtained with Gram's method. The specimen shows a dense network of mycelia, individual filaments of which are easily recognised at the periphery of the network. The filaments are long and very slender. No septæ could be made out, and it is difficult to determine whether any dichotomous division of the filaments takes place. Under the microscope these filaments appear identical with, but slightly thicker than, those of actinomyces. They differ from cladothrix alba and asteroides in having no septæ, and from cladothrix dichotoma in the absence of pseudo-division.

[1] *Hygienischen Rundschau*, 1894, No. 12.

When examined fresh these filaments appear to have a very thin cell wall and finely granular protoplasm. No spores have been observed, nor can any motion of the filaments be detected. From actinomyces[1] filaments they differ in the rapidity with which they take up aniline stains. Some of the filaments appear to be slightly bulbous at the end, but no spores can be detected at this part. They are very brittle, and on attempting to separate them they generally break up into short pieces.

While in Bombay one of us had the opportunity of examining fresh particles of the white variety, and the purulent discharge from the sinuses in cases placed at our disposal by Drs. Hatch, Parukh, and Nanavati. The fresh particles showed numerous acicular crystals, which were easily dissolved up by alcohol and ether, leaving the particles free, and thus clearly showing the radiating filaments of the fungus.[2] The fresh particles, when examined with Nicol's prisms, showed a peripheral zone which rotated polarised light. Particles, after being treated with alcohol and ether, did not show the same zone, thus proving that these reagents had dissolved away the crystalline structure. The discharge showed numerous oil globules and dark red pigment granules. On treating these granules with hypo bromide of soda solution, according to the method we applied for decolorising the particles found in the black variety of mycetoma, they did not lose the colour easily, nor did they show any fungus at all. On leaving them in ferricyanide of potassium solution for about fifteen minutes, and subsequently transferring to dilute nitric acid, the Prusssian blue reaction for iron was easily obtained. When treated in the same way with ferro-cyanide of potassium and dilute nitric acid a green colour was obtained. Some of the sections showed similar particles in the inflammatory area, and these also gave the same reaction. In one of the cases the chief peculiarity noticed was the invasion of the muscles of the leg thus converting them into bags full of the white particles.

Our attention was drawn to the question whether the lower animals suffered from a similar complaint or not. Dr. Goudinhoe, of Bombay, showed to one of us a small piece of

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[1] Dr. Carter and Dr. Kanthack.

[2] Dr. Carter and Drs. Lewis and Cunningham.

tissue excised from a horse suffering from a disease called the "kankir" or "barsati" growth. This disease generally appears during the rainy season, and thus it is called the "barsati growth." A chronic ulcer forms on one of the extremities, from which white particles are discharged. The term "kankir" is applied to the disease on account of the presence of these particles. The veterinary surgeons generally excise it, but the disease reappears often in the same part during the next rainy season. Secondary growths have been described as occurring in the lungs. An excised piece was examined by us for the presence of a fungus similar to the mycetoma fungus. The particles were very hard and horny. Pure nitric acid made them swell up and dissolve. Treating them with hybobromite of soda did not show any fungus, neither did sections of the tissue with the particles *in situ* show it. The fact of secondary growths in the lungs, however, points to the presence of an infective agent in these particles.

In conclusion, returning to the mycetoma fungus, we have only to state that inoculation experiments have not been as yet carried on with the cultivated organisms. Finally, we have to thank Professor Horsley and Professsor Childe, of Bombay, in whose laboratories the observations were made, and chiefly to H. H. the Dewan of Palanpur, for enabling one of us to carry on the work.

The PRESIDENT (Dr. Woodhead) thought that the special interest of the communication lay in the fact that it afforded additional evidence of the parasitic nature of Madura foot, which had so long been insisted upon by British pathologists in India. Although inoculation experiments had not been successful up to the present, there could be no doubt that the evidence of the parasitic nature of the disease was becoming stronger every day. The relation of the disease to a group similar to actinomycosis, and the identification, separation, and cultivation of an organism of the streptothrix group were all advances for which pathologists were deeply grateful to Dr. Surveyor and Professor Boyce.

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